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Investigations of adaptive neural networks were conducted using the classically conditioned nictitating membrane response (NMR) of rabbit. Work involved both neurobiological and theoretical approaches based on mathematical models and computer simulation. Recordings were done from single brain stem neurons in awake, behaving animals for the purpose of determining the loci and activity related to CRs. Computational tools for applying systems analysis to neurophysiological data obtained from single-unit recordings from awake behaving animals were developed. The relationship between single neurons' dynamic behavior and the CR in terms of differential equations and sophisticated correlational analyses based on Fourier and Laplace transform methods was characterized. Theoretical studies revolved around two mathematical models of learning. The Sutton-Barto-Desmond (SBD) model was designed to describe real-time features of the NM CR. A cerebellar network implementation of this model was constructed by combining parametric constraints of the model dictated by behavioral data with constraints based on anatomy and physiology of the cerebellum. The second OVER

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Final Technical Report
AFOSR 86-0182 (Adaptive Networks)
Dr William O Berry, Program Manager

Biological Investigations of Adaptive Networks: Neuronal Control of Conditioned Responses

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Unversity of Massachusetts, Amherst 01003

I. Summary

Investigations of adaptive neural networks were conducted using the classically conditoned nictitating membrane reponse (NMR) of rabbit, a widely used model system for studies of learning. Our work involved both neurobiological and theoretical approaches based on mathematical models and computer simulation. The primary experimental approach involved recording from single brain stem neurons in awake, behaving animals for the purpose of determining the loci and activity related to CRs. We developed computational tools for applying systems analysis to neurophysiological data obtained from single-unit recordings from awake behaving animals. With the acquisition of an expanded computer network, we became able to routinely characterize the relationship between single neurons' dynamic behavior and the CR in terms of differential equations and sophisticated correlational analyses based on Fourier and Laplace transform methods. A second experimental approach used WGA-HRP for anatomical studies of involved brain stem/cerebellar circuits. This work significantly adds to our understanding of neural circuits underlying NMR conditioning.

Theoretical studies resolved around two mathematical models of learning. One is the Sutton-Barto-Desmond (SBD) model which represents an implementation of the more general Sutton-Barto model. The SBD model was designed to describe real-time features of the NM CR. A cerebellar network implementation of this model was constructed by combining parametric constraints of the model dictated by behavioral data with constraints based on anatomy and physiology of the cerebellum. The second major theoretical development was the construction of a two-element neural-network architecture that elegantly describes adaptive timing as manifested in the fine-grain temporal characteristics of CRs. This model, designated VET in some of our papers, overcomes certain limitations of the SBD model. A proposed cerebellar implementation of this model is described in an appended report and in forthcoming published articles.

II. Research objectives

The general objectives for the reporting period were the same as those stated in previous reports going back to those submitted in connection with AFOSR Grant 83-0215. These goals and our approches to them remain unchanged, so no purpose would be served by restating them here. The status of work in the field and the contributions of our laboratory are summarized in technical reports listed in Section IV. I should mention that the experimental research outlined below was

partially supported by NSF. This grant provided some of the funds needed for equipment used in conjunction with single-unit recording and anatomical studies. Both AFOSR and NSF are acknowledged in our reports because funds from both agencies have been used to purchace general purpose equipment. There has been no duplication of effort in connection with these two sources of support.

III. Status of research

The main research efforts over the past three years are summarized in an appended manuscript by the Principal Investigator entitled "Implementing connectionist algorithms for classical conditioning in the brain". This article provides an overview of our experimental and theoretical efforts within the context of related work in other laboratories. It is not a complete description of all of our work, however; detailed summaries have been provided in prior semi-annual reports and published materials (Section IV).

Also appended is a paper entitled "Single-unit activity in the rabbit red nucleus during the classically conditioned nictitating membrane response: A preliminary report". This paper was included in this technical report because, unlike other single-unit recording studies performed in this laboratory during the past three years, it was not described in the proposal submitted last year which led to our current grant, AFOSR 89-0391.

Finally, this report lists computer softwareB created by members of our group over the past three years (Section VIIA).

IV. Technical reports

Included are published citations of work published and "in press" from 1986 to the present. Referencess from 1987 were *initiated* under AFOSR Grant 86-0182 and partially supported by NSF as explained in Section II.

1. Moore, J.W., Desmond, J.E., Berthier, N.E., Blazis, D.E.J., Sutton, R.S., Barto, A.G. Simulation of the classically conditioned nictitating membrane response by a neuron-like adaptive element: Response topography, neuronal firing, and interstimulus intervals. *Behavioural Brain Research*, 1986, 21: 143-154.

2. Blazis, D.E.J., Desmond, J.E., Moore, J.W., Berthier, N.E., Sutton, R.S, and Barto, A.G. Simulation of the classically conditioned nictitating membrane response by a neuron-like adaptive element: A real-time variant of the Sutton-Barto model. *Proceedings of the Eighth Annual Conference of The Cognitive Science Society.* Hillsdale, N. J.: Lawrence Erlbaum Associates, 1986, 176-186.

3. Schmajuk, N.A. and Moore, J.W. A real-time attentional-associative network for classical conditioning of the rabbit's NMR. *Proceedings of the Eighth Annual Conference of The Cognitive Science Society.* Hillsdale, N. J.: Lawrence Erlbaum Associates, 1986, 794-807.

4. Desmond, J.E., Blazis, D.E.J., and Moore, J.W. Computer simulations of a classically conditioned response using neuron-like adaptive elements: Response topography. *Society for Neuroscience Abstracts*, 1986, 12: 516.

5. Rosenfield, M.E. and Moore, J.W. HRP-WGA studies of premotor cerebellar-brain stem pathways for the classically conditioned nictitating membrane response. *Society for Neuroscience Abstracts*, 1986, 12: 752.

6. Berthier, N.E. and Moore, J.W. Cerebellar Purkinje cell activity related to the classically conditioned nictitating membrane response. *Society for Neuroscience Abstracts*, 1986, 12: 1418.

7. Berthier, N.E. and Moore, J.W. Cerebellar Purkinje cell activity related to the classically conditioned nictitating membrane response. *Experimental Brain Research*, 1986, 63: 341-350.

8. Desmond, J. E. and Moore, J. W. Dorsolateral pontine tegmentum and the classically conditioned nictitating membrane response: Analysis of CR-related single-unit activity. *Experimental Brain Research*, 1986, 65: 59-74.

9. Berthier, N.E., Desmond, J.E., and Moore, J.W. Brain stem control of the nictitating membrane response. In Gormezano, I., Prokasy, W.F., and Thompson, R.F. (Eds.), *Classical Conditioning, 3rd Edition.* Hillsdale, NJ: Lawrence Erlbaum Associates, 1987, 275-286.

10. Schmajuk, N.A. and Moore, J.W. *Two Attentional Models of Classical Conditioning: Variations in CS Effectiveness Revisited.* University of Massachusetts at Amherst, Department of Computer and Information Science, Technical Report 87-29, 1987, 33 pages.

11. Blazis, D.E.J. and Moore, J.W. *Simulation of a Classically Conditioned Response: Components of the Input Trace and a Cerebellar Implementation of the Sutton-Barto-Desmond Model.* University of Massachusetts at Amherst, Department of Computer and Information Science, Technical Report 87-74, 1987, 61 pages.

12. Moore, J.W. and Berthier, N.E. Purkinje cell activity and the conditioned nictitating membrane response. In Glickstein, M., Yeo C., and [illegible], J (Eds.), *Cerebellum and Neuronal Plasticity*, New York: Plenum, 1987, 339-352.

13. Desmond, J.E. and Moore, J.W. Red nucleus single-unit activity during the classically conditioned rabbit nictitating membrane response. *Society for Neuroscience Abstracts*, 1987, 13: 841.

14. Blazis, D.E.J. and Moore, J.W. A cerebellar cortical implementation of the Sutton-Barto-Desmond model of the classically conditioned rabbit nictitating membrane response. *Society for Neuroscience Abstracts*, 1987, 13: 842.

15. Desmond, J.E. and Moore, J.W. Adaptive timing in neural networks: The conditioned response. *Biological Cybernetics*, 1988, 58: 405-415.

16. Desmond, J.E. Temporally adaptive conditioned responses: Representation of the stimulus trace in neural-network models. University of Massachusetts at Amherst, Department of Computer and Information Science, Technical Report 88-80, 1988, 52 pages.

17. Schmajuk, N.A. and Moore, J.W. The hippocampus and the classically conditioned nictitating membrane response: A real-time attentional-associative model. *Psychobiology*, 1988, 16: 20-35.

18. Berthier, N.E., Barto, A.G., and Moore, J.W. Linear systems analysis of cerebellar deep nuclei cells during performance of classically conditioned eyeblink. *Society for Neuroscience Abstracts*, 1988, 14: 1239.

19. Rosenfield, M.E. and Moore, J.W. Is there a reciprocal connection between red nucleus and interposed cerebellar nuclei in rabbit? *Society for Neuroscience Absracts*, 1988, 14: 493.

20. Moore, J.W. and Blazis, D.E.J. Cerebellar Implementation of a Computational Model of Classical Conditioning. In Strata, P. (Ed.), *The olivocerebellar system in motor control.* Berlin: Springer-Verlag, 1989, 387-399.

21. Moore, J.W. and Blazis, D.E.J. Simulation of a classically conditioned response: a cerebellar neural network implementation of the Sutton-Barto-Desmond model. In Byrne, J. H. and Berry, W. O. (Eds.), *Neural models of plasticity. Experimental and theoretical approaches.* New York: Academic Press, 1989, 187-207.

22. Moore, J.W. and Blazis, D.E.J. Conditioning and the cerebellum. In Arbib, M.A. and Amari, S. *Dynamic interactions in neural networks: Models and networks.* Berlin: Springer-Verlag, 1989, 261-277.

23. Schmajuk, N.A. and Moore, J.W. Effects of hippocampal manipulations on the classically conditioned nictitating membrane response: simulations by an attentional-associative model. *Behavioural Brain Research*, 1989, 32: 173-189.

24. Moore, J.W. Cerebro-cerebellar learning loops and language. Peer commentary, *Behavioral and Brain Sciences*, 1989, 12: 156.

25. Moore, J.W. and Desmond, J.E. A cerebellar neural network implementation of a temporally adaptive conditioned response. In Gormezano, I. (Ed.), *Learning and memory: The biological substrates.* Hillsdale, NJ: Lawrence Erlbaum Associates. In press.

26. Coulter, D.A., Lo Turco, J.J., Kubota, M., Disterhoft, J.F., Moore, J.W., and Alkon, D.L. Classical conditioning reduces the amplitude and duration of the calcium-dependent afterhyperpolarization in rabbit pyramidal cells. *Journal of Neurophysiology*, 1989, 61: 971-981.

27. Moore, J.W., Desmond, J.E. and Berthier, N.E. Adaptively timed conditioned responses and the cerebellum: A neural network approach. *Biological Cybernetics.* In press.

28. Moore, J.W. Implementing connectionist algorithms for classical conditioning in the brain. In Commons, M., Grossberg, S., and Staddon, J.E.R. (Eds.), *Neural network models of conditioning and action.* Hillsdale, N.J.: Lawrence Erlbaum Associates. In press.

29. Moore, J.W., Berthier, N.E., and Blazis, D.E.J. Classical eye blink conditioning: Brain systems and implementation of a computational model. In Gabriel, M and Moore, J.W. (Eds.), *Learning and computational neuroscience.* Cambridge, MA: MIT Press. In press.

V. Professional personnel

1. John W Moore, Ph D, Psychology (Experimental/Learning), Indiana University, 1962. Professor of Psychology (Biopsychology); Core Faculty, Neurosciece and Behavior (NSB) Program ; Associated Professor of Computer and Information Science.

2. Neil E Berthier, Ph D, Psychology (Neuroscience and Behavior), University of Massachusetts, 1981. Senior Research Associate. Dr Berthier serves as a resource person and colleague. His salary has been provided by NSF Grant BNS 85-06787, on which he is co-PI.

3. John E Desmond, Ph D, Psychology (Neuroscience and Behavior), University of Massachusetts, 1985. Research Associate.

4. William G Richards, Ph D, Pychology (Neuroscience), Princeton University, 1985. Research Associate.

5. Marcy E Rosenfield, B S (Zoology), University of Massachusetts, 1982. Rosenfield's formal title is Departmental Assistant. She is a certified AALAS animal care technician.

VI. Interactions

Unless otherwise specified, the professional interactions listed in this section refer to the PI. The material is broken down by year. The listings from Years One and Two are taken verbatim from previous annual technical reports.

Year One:

1. Slide session chairperson and member of the program committee, Eighth Annual Conference of the Cognitive Science Society, University of Massachusetts - Amherst, August, 1986.

2. Poster presentations, etc., Society for Neuroscience meetings, Washington, D C, November, 1986.

3. Participant in plenary session on Cerebellum and Learning (with R F Thompson, W Welker, and S G Lisberger), Winter Conference on Neurobiology of Learning and Memory, Park City, Utah, January 1987.

4. Speaker at Conference on Neural Models of Plasticity, Woods Holes MA, April-May, 1987.

5. Speaker and Participant at U S - Japan Seminar on Competition and Cooperation in Neural Nets 2, University of Southern California, May, 1987.

Other principal interactions involve ongoing interactions (e g, classes and seminars) and collaborative relationships with colleagues: A G Barto, R S Sutton, M Jordan, A H Klopf, E J Kehoe, N A Schmajuk, J Ayres, and others.

Because it involved grant supported travel, I should specifically note that J E Desmond, D E J Blazis (graduate student), and I visited A H Klopf at Wright Aeronautical Laboratories for two days in June, 1986 to conduct simulation studies of Klopf's drive-reinforcement model and R S Sutton and A G Barto's time-difference model (formerly known as the adaptic heuristic critic element).

Year Two:

1. Principal Participant: Satellite Symposium of the 2nd IBRO World Congress of Neuroscience, *The Olivocerebellar System and Motor Control*, Turin, Italy, August, 1987.

2. Invited colloquia and seminars during 1987-88 academic year: Wesleyan University, University of Texas, University of Illinois.

3. Presentations at meetings: AFOSR Life Science Program Review, Brooks AFB, Texas, December, 1987; Annual Winter Conference on Neurobiology of Learning and Memory, Park City, Utah, January, 1988; Invited lecture, Midwestern Psychological Association meetings in Chicago, April, 1988.

4. Grant Panels Activity: NIH Biopsychology Panel (ad hoc), October, 1987. This included site visits to UCIrvine and UCLA during September, 1987; NIMH Behavioral Neurobiology Subcommitee (ad hoc), October, 1987; NSF panel on Research Experiences for Undergraduates (Psychobiology sub panel), February, 1988; ONR program review in Cognitive and Neural Science (Board of Visitors), February, 1988.

5. Reviewing and Related Activity: Consulting editor for *Psychobiology* and reviewed manuscripts for *Journal of Experimental Psychology: Animal Behavior Processes*, *Psychological Bulletin*, *Behavioral Brain Research*, MIT Press. Member of Advisory Board for a new monograph series, *Research Notes in Neural Computing*, to be published by Springer-Verlag.

6. I was honored in being asked to nominate possible recipients of this year's Kyoto Prize (a Nobel class monetary award given by Japan's Inamori Foundation) for work in Cognitive Science. The prize was ultimately awarded to Noam Chomsky.

7. Continuing strong interactive relationships with A G Barto and other colleagues working in Adaptive Networks: A H Klopf's group at Wright-Patterson, R S Sutton at GTE Labs, N A Schmajuk presently at Northwestern University and others.

8. Our relationship with Barto's group continues to strengthen our relationship with the university's Department of Computer and Information Sciences where I am Associated Professor.

9. Drs Berthier and Desmond became Associated Faculty of the university's NSB Program. They have also been asked to review grant proposals and submitted manuscripts.

Year Three:

1. Perhaps the most significant interactions occurred as part of team-taught graduate level seminar offered by my colleague in computer science and myself (COINS 891A, fall, 1989, 3 credits). The genernal topic was behavioral, biological, and computational approaches to learning.

2. The fall of 1988 also provided opportunities for substantial interaction with Dr James Houk, a cerebellar and motor system physiologist who is chair of the physiology department at Northwestern University Medical School. Dr Houk spent part of his sabbatical semester here, and interactions with him were mutually rewarding in two main areas: (a) quantitative treatment of neural neural data related to movement—especially systems analysis; (b) cerebellar implementation of computational models.

3. I gave a major invited presentation at a satellite symposium organized by D. Alkon and C. Woody held in connection with the 1988 meetings of the Society for Neuroscience in Toronto.

4. I gave an invited talk at the annual Winter Conference on the Neurobiology of Learning and Memory convened at Park City, Utah, January, 1989.

5. I gave an invited talk to the neuroscience group at Oxford University in March, 1989.

6. I gave an invited lecture at the Twelfth Symposium on Models of Behavioral convened at Harvard University, June, 1989.

7. Neil Berthier gave an invited talk in the department of neurobiology at SUNY Stony Brook, February, 1989.

8. John Desmond gave an invited talk to the psychology department of Brown University in March, 1989.

9. Diana Blazis (graduate student now working on her dissertation) gave an invited talk to the psychobiology group of Yale University, May, 1989.

VII. New discoveries

Discoveries that might be designated as new were those stemming from experimental research, e.g., the anatomical work discussed above in published and forthcoming technical reports.

VIIA. Software developed

Most of the software developed over the past three years was designed to run on our local network of Sun workstations (SUN LAN), which includes a DEC LN03-plus laser printer, dumb terminals, and interfaces for Apple IIe and other small systems. Summaries of software written by Neil Berthier, Diana Blazis, and Bill Richards appear below.

Additional software has been written by John Desmond. Because of its length, Desmond's summary appears as a separate appendix to this report.

Software by Neil Berthier:

Dr Berthier has done most of the system programming. and he has created several programs for performing sophisticated analyses of neural and behavioral data.

- Upgrade SunOS software as it became available, applied patches as necessary.
- Install X window system, with Purdue patches. Install and debug contributed software including: x-graph-11, texx2.9, xlock, xviewsun, xgdb, twm, xdbx, xfig.
- Install and debug text formating and printing software based on TeX, LaTeX, BibTex, SliTex, dvi2ln03, ln03dvi, dvitool. Write LaTeX macros.
- Install Gnu software, gnu-gcc, gnu-gdb, gnu-emacs. Write macros for gnu-emacs.
- Write a graphics driver for DEC ln03-plus.
- Write a system of programs to do basic analysis of spike data.
  - periresponse.c – compute periresponse histograms.
  - mannwhit.c – test null hypothesis about firing patterns using a Mann-Whitney test.
  - kolsmir.c – test null hypothesis about firing patterns using a Kolmogorov-Smirnow test.
  - binom.c – test null hypothesis about firing patterns using a Binomial test.
  - prelim.c – compute basic parameters of cell firing and test null hypothesis about firing patterns using a poisson test.
  - gamm.c – test null hypothesis about firing patterns using a gamma distribution hypothesis.
- A system of programs to compute digital filter coefficients, and to digitally filter data.
  - kaiser.c – compute kaiser filter coefficients.
  - marr.c – compute Marr-Hildreath filte coefficients.
  - filter.c – filter spike data with digital filter.
  - filterdis.c – display filtered data using SunView.
  - perifil.c – display periresponse filtered data.

- A system of programs to do fast Fourier transforms (FFTs).
  - fft.c – do foward FFT.
  - ifft.c – do inverse FFT.
  - fdat.c – do FFT of data.
  - fftdis.c – display FFT of data.
  - fcoef.c – do FFT of filter coefficients.
- A system of programs to do linear systems analyses of data.
  - recur.c – a program that computes time series analysis coefficients by inverting matrices.
  - convolv.c – use periodic convolution to get predicted output of the linear system.
  - mserr.c – compute multiple R.
  - correlation.c - use FFT and iFFT to do cross-correlational analysis.
  - disp-correlation.c - display results of cross-correlation with SunView.
  - transf.c – compute transfer function for a set of coefficients.
  - transdislog.c – display and fit transfer functions using SunView.
- A system of programs to compute time series coefficients using QR decomposition.
  - recur_main.c – main program to compute coefficients.
  - QRdecomp.c – programs based on LINPACK to do QR decomposition using Householder transformations.
  - float_signal.c – catches floating point errors.
- Many Unix scripts to resolve systems problems.

Software by Diana Blazis:

- **General Simulator.** Computes inputs, outputs and update rules for models of adaptive behavior. The program can be run interactively or automatically ("batch" processing). In interactive mode the program provides popup menus which allow the user to change learning algorithms, model parameters, and learning procedures at will. The program displays the appearance of the paradigm, computes the experiment, and plots model output in several forms. In batch mode, the program reads prepared command files and automatically generates hardcopy graphics output on request. Presently, the simulator runs several learning algorithms for many different stimuli. The modular form of the simulation program allows for future incorporation of other learning rules. Graphics output, which includes response waveforms for acquisition and terminal trials, learning curves, and spike histograms, can be enabled or disabled at operator request.

- **nmrtool**. Interactive program for analysis of data obtained during classical conditioning trials. Data collected using our Apple First system are written to disk and then uploaded to the SUN LAN. nmrtool displays responses for all trials. Several response measures are computed, including peak and onset latencies, CR amplitudes, and CR areas. Learning curves are plotted. Hardcopy of nmrtool results is available at user request. nmrtool generates summary files that used for automated statistical analysis of the data. Future plans for nmrtool include a user interface to program analysis of data obtained during any classical conditioning procedure.

- **Related projects**. (a) Basic nmrtool: used prior to the implementation of nmrtool for the SUN LAN. Data from behavioral experiments were analyzed on our Apple IIe's using a modifified version of an analysis program prepared by John Desmond and Bill Richards. (b) File conversion routines: data obtained from the FIRST system that controls behavioral experiments via Apple IIes and collects data must be converted for transfer to the SUN LAN. File conversion is coded in Basic and executed on the Apple IIe. (c) Applications programming and maintenance for our FIRST system, e.g. programming stimulus control for new experiments. (d) Assorted small programs for statistical manipulation of output files of nmrtool.

Software by Bill Richards:

Dr Richards wrote software that enables a Commodore C-64 computer to control physiological recording experiments. This software is readily transferable to other computers using the 6502-series 8-bit processor.

- **Acq/ctrl**. This program is a BASIC/assembly language hybrid that controls CS and US presentations for differential conditioning, detects CRs, counts neural spikes in two separate channels, and provides on-line cumulative histograms of spike activity compiled separately for CS+ and CS- trials and for CR and non-CR trials.

- **EVENT**. Assembly language program for off-line trial-by-trial analysis of event timing. Events on eight channels are timed with 0.1 msec resolution. The program also controls A/D sampling of voltage trace from NMR transducer and disk files for NMR, neural spikes, and synchronization.

- **HSAD**. Basic/assembly language program which controls high-speed digitization of a single channel of neural spike activity for (a) confirmation of window discrimination (reads and edits corresponding disk files generated by EVENT) or (b) graphic plotting.

- **FORMAT** Converts EVENT files downloaded from C-64 to format which ANALYZE (by John Desmond) can read.

- **FIG.HIRES** Reads C-64 HSAD files and EVENT NMR files and generates oscilloscope-like figures showing neural activity and NMR for single trial on laser printer (LN03). An example

is shown in Figure 1. Previously, such illustrations required costly and time consuming photographic processing.

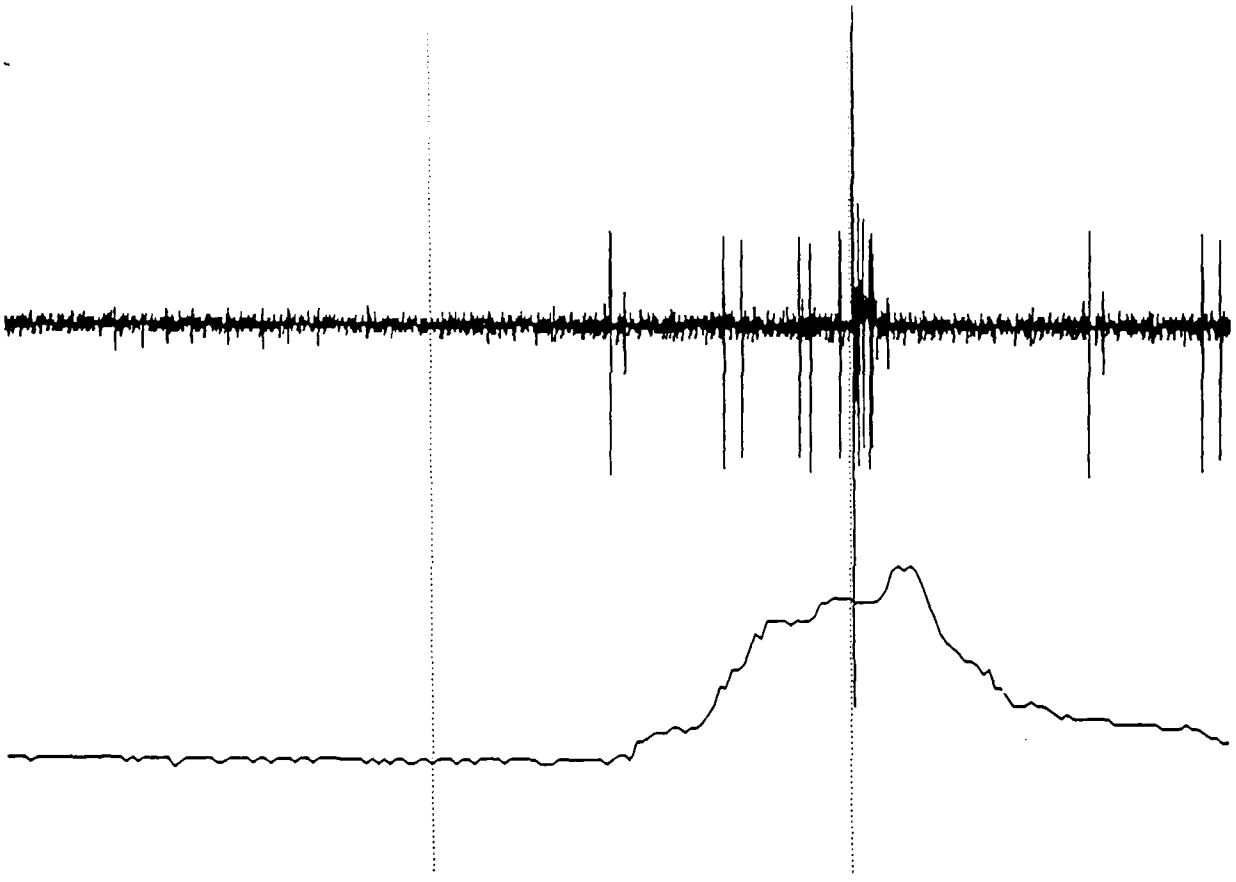

Figure 1. Illustration of FIG.HIRES output. Top trace is single-unit neural activity on a single NMR conditioning trial. The second trace is the corresponding NMR. The left-hand dashed vertical line represents CS onset. The right-hand vertical line represents US onset. The interval between the two lines is 350 milliseconds.

John E. Desmond – software development

C/Unix software for the Sun

iball is a mouse-driven SunView program that allows user to examine individual trials from a recording session. The CR, spikes, cumulative sum of spikes, and the cumulative sum adjusted for baseline firing is displayed. By using the mouse, the CR onset, CR duration, CR velocity, burst onset, burst duration, burst velocity, and burst depth of modulation is computed and displayed. In addition, CR area and maximum CR amplitude are automatically computed. The data can be stored for further analyses and subsequently reloaded for modifications. The user also has option of displaying the following averaged plots: (a) CS+ or CS- trials (b) CR trials (c) NO CR trials, (d) CR trials adjusted for CR onset. Sample output is depicted in Figures 1, 2, and 3.

binom performs binomial statistical test on CR and NO CR trials. Tests the null hypothesis that firing rate is identical for the two trial types within a specified time interval, as described by Dorrscheidt (1981).

plot_isi outputs interspike interval histograms of cell baseline firing. The output is stored in a file in a way that can be easily searched with standard Unix search functions.

cusums generates the following graphical display (SunView) for 5 cells at a time: (a) averaged PSTH for CR trials, (b) averaged PSTH for NO CR trials, and (c) averaged PETH for CR trials. The number of trials for each graph is also displayed. The user has the option to include or remove time calibration grid. The program can also be set up in an autoprint mode for batch printouts of all cells.

ave_changepoint (in collaboration with Neil Berthier) displays averaged filtered neuronal activity for CR and Non-CR trials. Filtered waveforms are displayed in a peristimulus plot (synced to the CS onset) and in a perievent plot (synced to the CR onset). Nine cells are displayed per screen, and screens can be printed out as batch job in autoprint mode. The purpose of the software is to find the time(s) at which neuronal firing rate changes. These times can be measured from the zero-crossing points of the waveform.

simdata simulates CRs and spikes. The program is designed to simulate neuronal activity that is *stimulus-dependent*, *movement-dependent*, or both. Activity that is movement-dependent can respond to the position, velocity, or acceleration of the movement, and can either lead or lag the simulated CR. Stimulus-dependent activity

occurs at a fixed latency relative to the onset of the CS. The purpose of this program is to generate data with known input-output properties for comparison with genuine data.

classify allows user to place cell numbers into different category files. The program is basically designed for data organization.

plot_cells is a mouse-driven CGI program for digitizing recording site locations. An anatomical atlas is drawn on the screen. The user then marks the recording location by pressing a mouse button, and the coordinates of the recording site are stored.

display_cells displays specified recording sites on screen atlas, using the coordinates generated in the "plot_cells" program. Sample output is depicted in Figure 4.

bib is a reference collection and formatting program. The program extracts references from a document and then generates a bibliography in the journal's preferred format.

findref is a database search program. The user enters key words and the program returns references that contain those keys.

raz is a SunView program for manipulating raster files on a simulated sheet of 8.5 X 11.0 inch paper. The user can adjust the position of multiple raster images and create a composite picture. The simulated sheet of paper can be rotated, and the images can be magnified or reduced. When the desired composite picture is achieved, a "snapshot" of the picture can be taken and printed on a LN03 laser printer. Sample output is depicted in Figure 5.

mmolar is a neural network model of classically conditioned responses. The program generates graphical (CGI) display of CR topography and synaptic weights. (See Desmond, 1988; Desmond, in press; Desmond and Moore, 1988; Moore, Desmond, and Berthier, in press).

fanout simulates spreading activation in a planar array of neuron-like elements. See pp. 33–43 in Desmond (1988).

nmr (in collaboration with Diana Blazis) is a SunView application for displaying and analyzing nictitating membrane response behavioral data collected on the APPLE FIRST system.

BASIC/Assembly Language software for Apple IIe

makefiles converts FIRST-formatted data into binary files that are suitable for uploading to the Sun.

spktime is an interrupt-driven assembly-language program that reads information from 3 tracks of a magnetic (VCR) tape. The first track contains analog (behavioral) information. The program digitizes this information at 5 ms intervals. The second track consists of neuronal events (action potentials). The program records the times at which the action potentials occur to 250 microsec accuracy. The program decodes trial type information and synchronous pulses from a third track. Data are stored on floppy disks and uploaded to a Sun workstation for subsequent analyses. The program queries the user for the starting and ending values of the tape counter for each cell, and stores this information in a file; thus, the experimenter obtains a comprehensive record of taped data that facilitates later retrieval.

Pavlov is a BASIC/assembly language program for running classical conditioning experiments on the Apple IIe while performing neurophysiological recordings. The program presents various conditioned and unconditioned stimuli to the subject, and codes each trial type presented on one track of a VCR magnetic tape. The trial types that are presented to the subject can be changed during the session with the press of a key. The number and types of trials presented are displayed on the monitor. Subject numbers and training protocols are stored to minimize errors in training. The program has a "collision mode" for perfoming neurophysiological collision experiments. In this mode, the computer is interfaced with a window discriminator. TTL output from the discriminator (caused by a spontaneously occurring action potential) is detected and this output triggers an oscilloscope sweep and initiates a precisely timed delay-interval (delay controlled by the experimenter). At the end of the delay, the computer triggers 2 stimulation pulses. If only the second of these pulses evokes an antidromic response, then the first stimulation pulse has collided with the spontaneously occurring spike.

I modified the Apple version of the public domain software "kermit" so that an entire disk's data can be uploaded, rather than one file at a time. This significantly reduces the amount of time that the user must devote to uploading.

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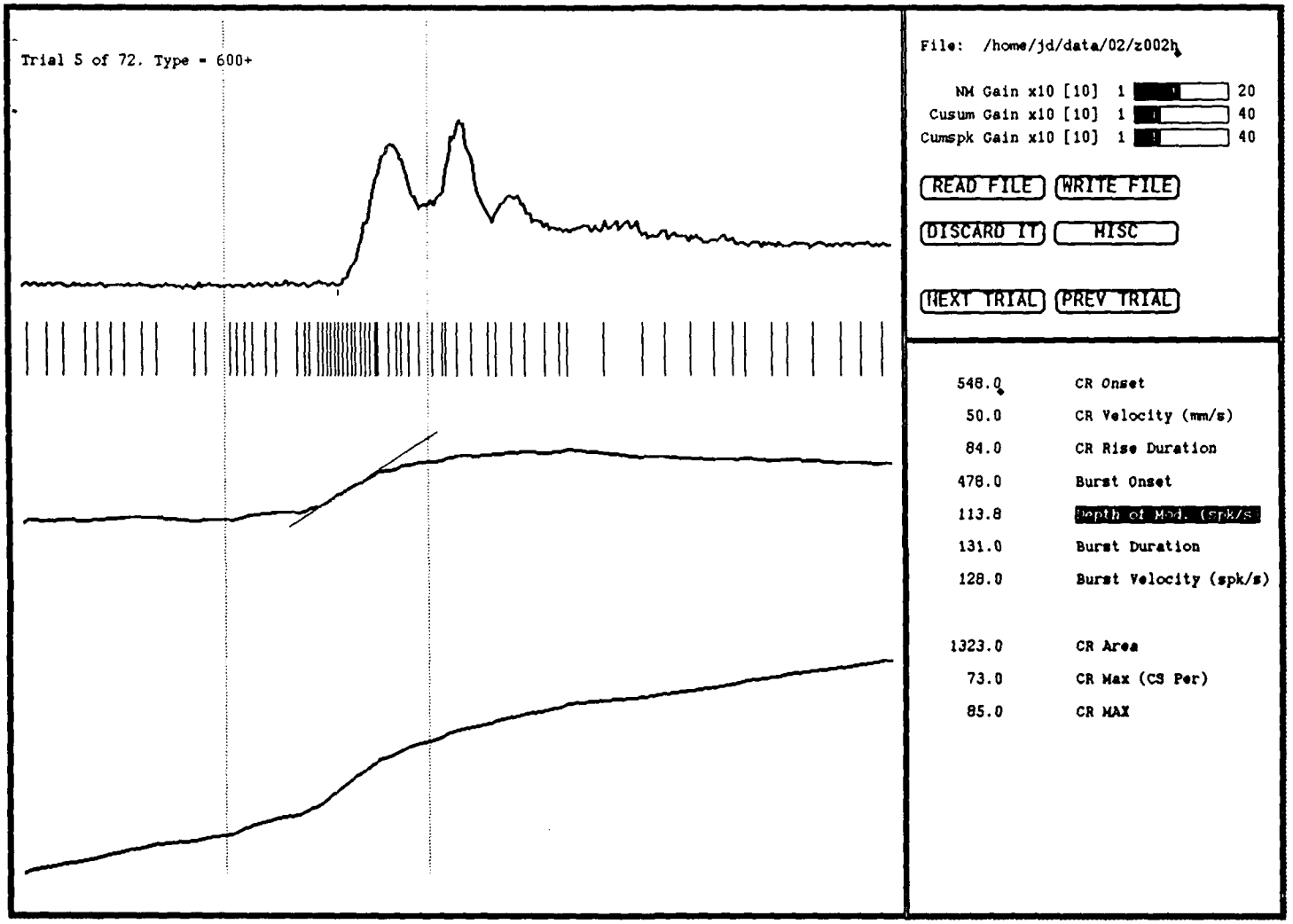

Figure 1: A single trial displayed in the iball software. The traces dsiplayed are, from top to bottom, digitized behavioral response, spike train, cusum, and cumulative spike counts. The two vertical lines represent, from left to right, CS onset and US onset. The straight line fitted on the cusum graph was drawn by the user. From the slope of this line, the software computes the depth of modulation of the neuronal burst. On this trial, the neuronal burst is firing at 113.8 spikes/sec above the baseline firing rate.

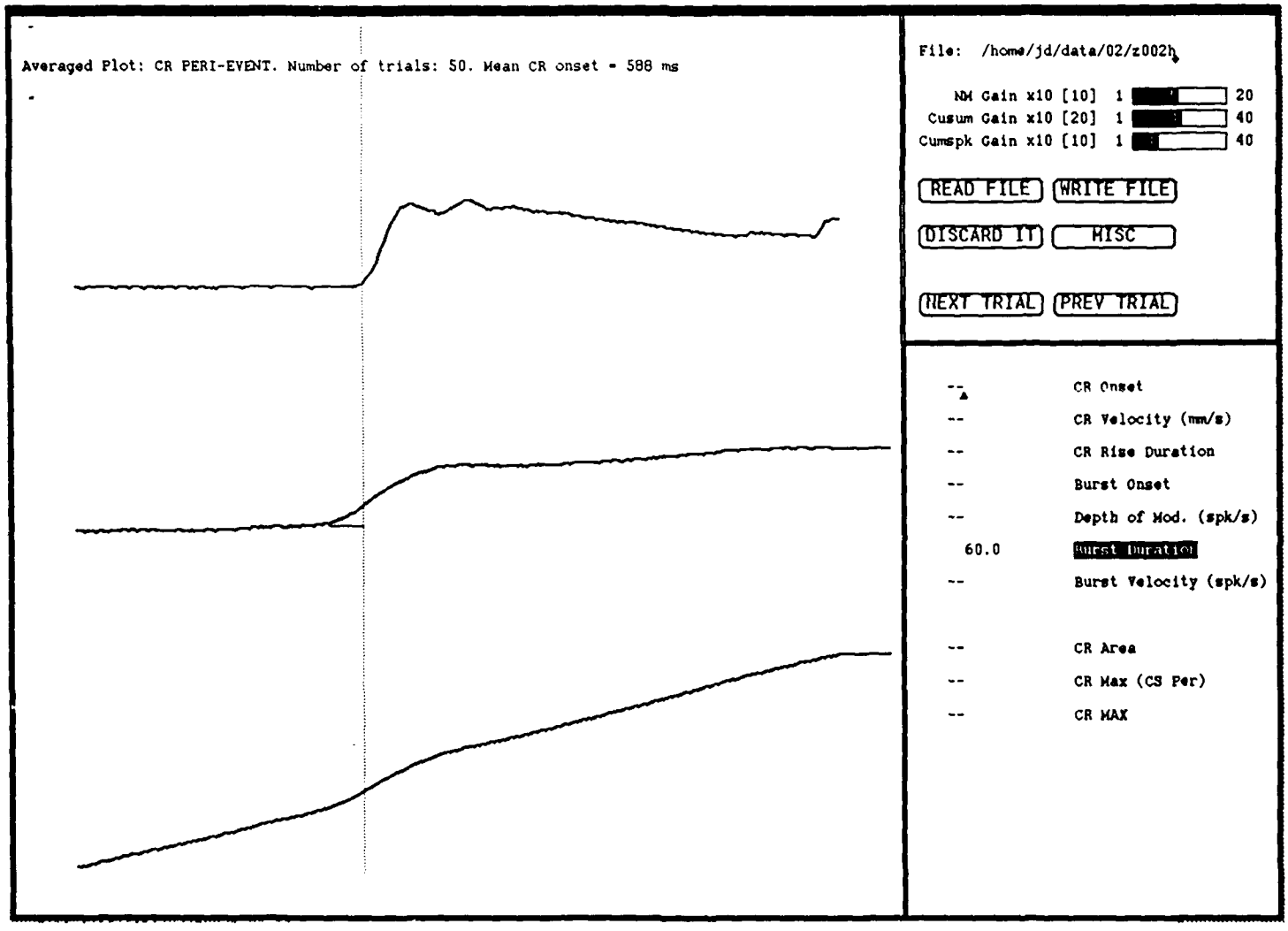

Figure 2: Output from the **iball** software. Depicted is behavior, cusum, and cumulative spikes averaged over all CR trials. Traces are synchronized to the CR onset (vertical line). From this plot, the user can estimate temporal relationship between neuronal activity and the behavior. In this example, neuronal firing precedes the behavior by 60 ms.

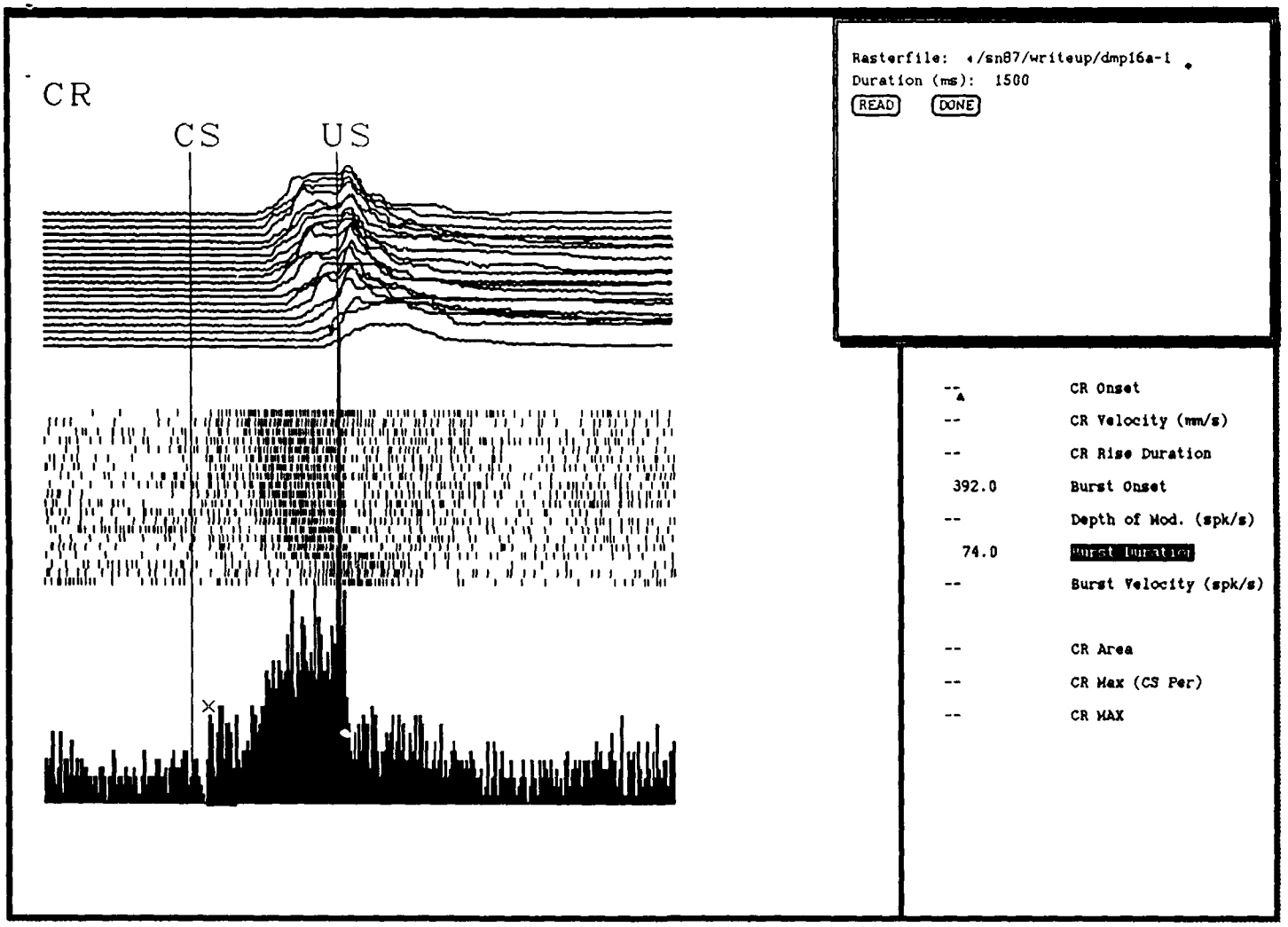

Figure 3: The raster mode of the **iball** software allows user to take advantage of **iball's** time measurement functions on graphs generated from other programs. In this example, the user has measured a CS-evoked burst of activity beginning at 392 ms and lasting for 74 ms.

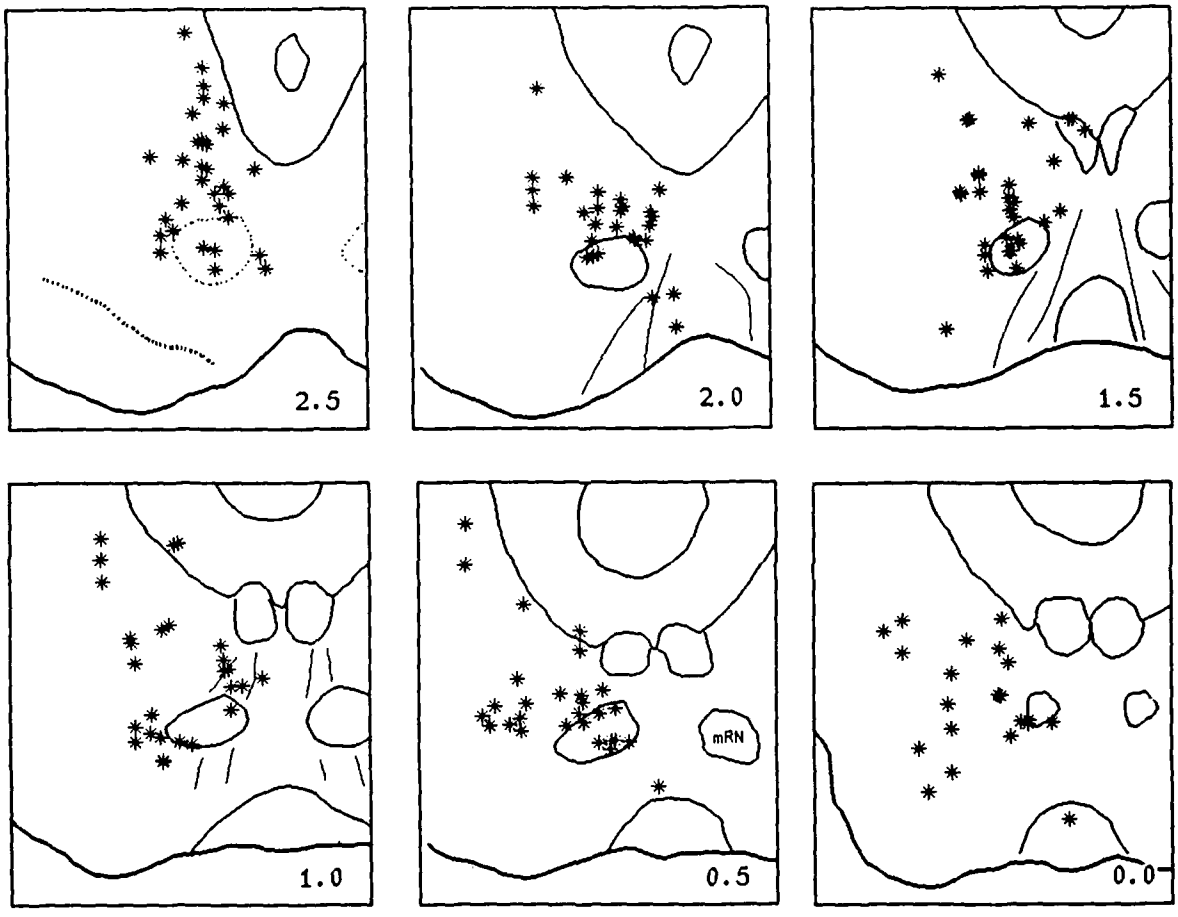

Figure 4: Output from the **display_cells** software. Coordinates of all cells, which have been obtained with the **plot_cells** software, are retrieved and cell positions are designated by asterisks. The user can display any subset of the cell population by entering those cell numbers. The program also has an extraction function. With this function the user specifies a region on the screen and the numbers of all cells that are located within the region are printed out.

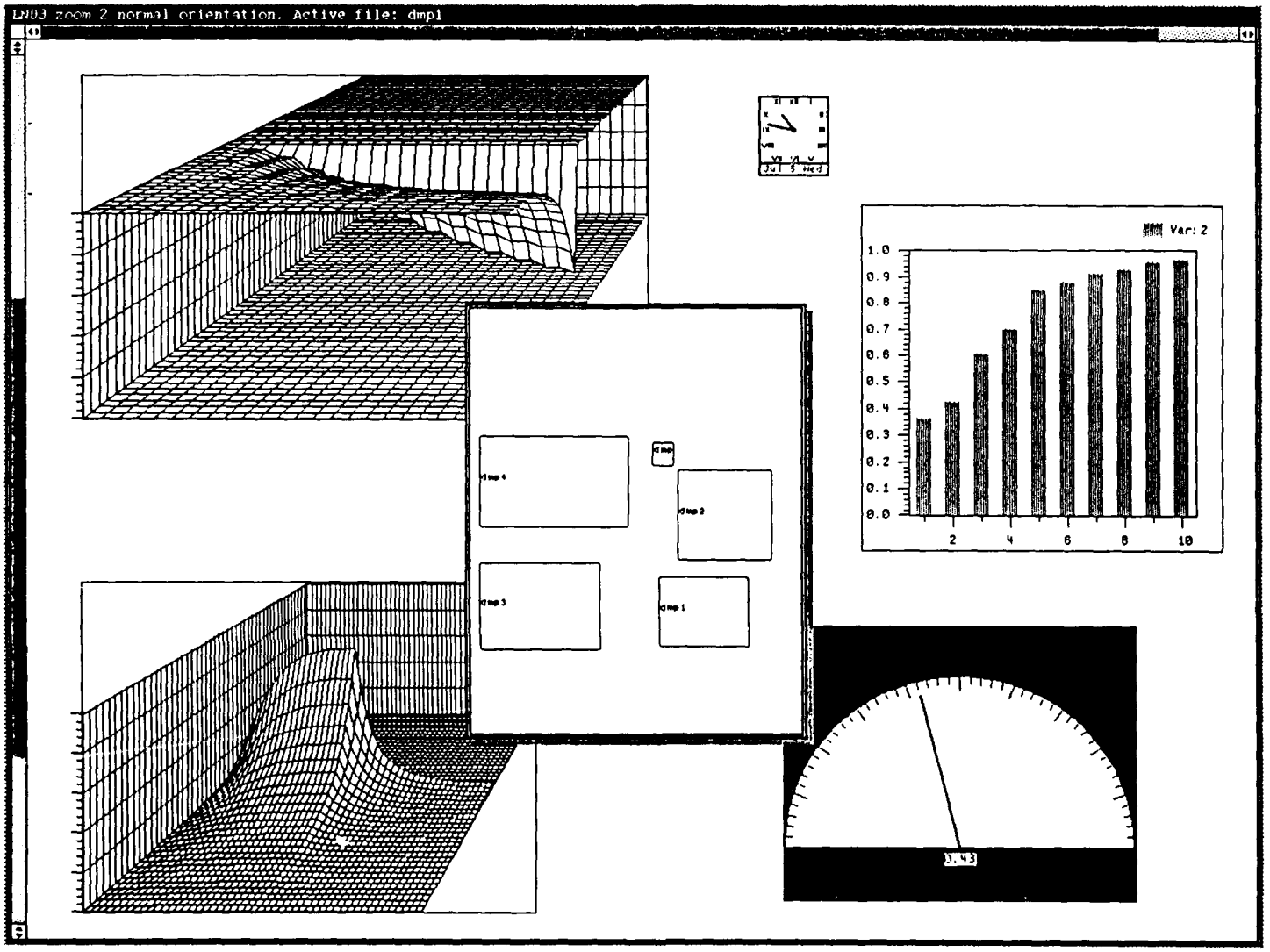

Figure 5: An example of the **raz** software. This figure illustrates 5 raster images on the screen. The screen can be scrolled up/down and right/left using the scrollbars. In the center of the display is a miniature view of the positions of the raster images as they would appear on an 8.5 in. by 11.0 in. sheet of paper. (This miniature view can be moved or hidden by the user). The images can be enlarged or reduced, and the page can be rotated. The user can select an image and change its position by moving the mouse cursor and pressing a button. When the user is satisfied with the positions of the images, a "snapshot" of the composite picture can be made and sent to the printer.

Implementing Connectionist Algorithms for Classical Conditioning in the Brain

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Implementing Connectionist Algorithms for Classical Conditioning in the Brain

Abstract Simple connectionist models of learning that conform to the Widrow-Hoff rule can be parameterized and extended to describe real-time features of classical conditioning. These features include the dependence of learning on the moment-to-moment status of input to the computational system and on the desired topography of its output. Using the classically conditioned nictitating response (NMR) of the rabbit as a prototypal system, my coworkers and I have devised models which successfully meet these real-time criteria. Two models and neural network architectures are described. The first consists of a single neuron-like processor with learning rules based on the Sutton-Barto model. The second consists of two neuron-like units with input based on a tapped-delay line representation of stimuli. Using anatomical and physiological data, both network models can be aligned with brain stem and cerebellar circuits involved in classical NMR conditioning. These models and their implementation in the brain have testable empirical consequences.

1. Introduction

This chapter illustrates how computational models based on abstract neural networks can provide insights into questions such as where in the brain learning occurs and the mechanisms that bring it about. It serves as a tutorial on aligning quantitative learning theory with physiology, thereby establishing a potential conduit for communication between molar and molecular levels of analyses. One might say that such efforts are about bringing abstract models to life in real nervous systems. Specifically, it brings together two lines of research: (a) studies of brain circuits underlying classical conditioning of a simple skeletal response, the rabbit nictitating membrane response (NMR) and (b) developing computational models applicable to real-time conditioning phenomena such as response topography and CS–US interval effects. Our work stands on a foundation provided by the "extended laboratory" (Gabriel, 1988) of those who investigate classical eye blink/NMR conditioning (Gormezano, Prokasy, and Thompson, 1987).

This chapter also illustrates Churchland's (1986) point that a theoretical dimension can be added to the neurosciences through a process of coevolution. Theories, expressed as computational algorithms, can guide decisions about where best to invest experimental resources. Behavioral neuroscientists regard the preparations they investigate as model systems, and therefore they are not indifferent to the broader implications of their work. However, they believe that exploiting these implications requires understanding the model system at multiple levels. At the computational level, this understanding is expressed in terms of algorithms capable of simulating how the system behaves under a range of environmental challenges. Production systems have this capability. More interesting and useful in the long run are algorthims that *emulate* what actually occurs in the brain to cause the system behave as it does.

I shall recount some of the steps my colleagues and I have taken in evaluating models of classical conditioning and casting them in terms of neural networks that might convincingly be implemented in real brains. By this I refer to discovering *alignments* between models and what is known of the anatomy and physiology underlying a given CR. I say "a given CR" because we are concerned primarily with developing theoretical frameworks useful to neuroscientist. As neuroscientists, our interest in theory cannot stray very far from the nuts and bolts of our experimental work. As neuroscientists, workers in the extended NMR conditioning laboratory seek a deep understanding of classical conditioning. Such an understanding demands rigorous theoretical expression, and thus NMR conditioning has been approached from three directions—behavior, biology, and computation. The overriding objective is to integrate these approaches in much the same way that oculomotor physiologists have done with saccadic eye movement and vestibular oculomotor reflexes (Robinson, 1981; 1989). The oculomotor example is apt because of shared anatomical systems.

Before proceeding, some comment about the title is in order. The title speaks of *implementing* connectionist algorithms[1] in the brain. Others have applied the term *instantiation* to this process. When considering the dictionary definitions of these two terms, I find implementation more apt. According to *Webster's New Collegiate Dictionary*, the infinitive "to instantiate" means "to represent an abstraction by a concrete example" whereas "to implement" means "to provide instruments or means of expression".

I would argue that instantiation is a prerequisite to implementation. To illustrate, my colleagues and I began by selecting one abstract computational theory, the Sutton-Barto (SB) model, which showed promise in describing many of the basic phenomena of classical conditioning, particularly the molar features of classical conditioning of the eye blink/NMR (Barto and Sutton, 1982; Sutton and Barto, 1981). We then sought a specific *instance* of the SB model which could describe in detail real-time features of the conditioned NMR, including response topography. We have referred to the resulting constrained and parameterized version of the model as the Sutton-Barto-Desmond (SBD) model (Moore, Desmond, Berthier, Blazis, Sutton, and Barto, 1986). By common usage, the SBD model is an *instantiation*—a concrete representation—of the abstract SB model. When we speak of implementing this model (Moore and Blazis, 1989), we mean finding brain processes and mechanisms ("instruments") conceivably capable of generating and explaining the measurable consequences of its parameterized and algorithmic ("instantiated") form.

Animal learning theorists are accustomed to evaluating models solely by behavioral criteria. They also prefer models that are parsimonious and elegant. Difficulties arise when there are many serviceable models to account for phenomena at the level of behavior. The instantiation of models into algorithmic and parameterized form adds constraints to models that are useful in their evaluation, but even at this level of exactness the choice of the more valid model can be arbitrary. Animal learning theorists attempt to escape from this dilemma by designing elaborate experiments that test highly refined behavioral predictions. While not minimizing the importance of this strategy, I suggest that a brain implementation scheme can imply independent experimental assessments of models using criteria at the level of neurobiology as an adjunct to behavioral criteria. It goes without saying that the success of this approach depends on having accurate information about neural substrates of the behavior being modeled. Implementations schemes should be physiologically compelling, not merely plausible. Later on I will illustrate this point by showing how implementation schemes my colleagues and I have devised for two models have testable hypotheses in the domain of neurophysiology. The situation is somewhat comparable to neuroanatomists' quest for Renhaw cells, which was stimulated by physiologists' claims that they must exist.

[1]Connectionist algorithms refer to any member of a class of models cast in terms of modifiable connection weights among neuron-like processing elements. The term is not limited to the so called delta or LMS learning rule or to learning through back-propagated error correction.

Devising good implementation schemes for instances of mammalian behavior such as NMR conditioning is not easy. It is difficult because of the virtual impossibility of obtaining direct and rigorous proof that mechanisms proposed to account for phenomenology actually exist and function in ways consistent with the model. We must therefore approach the question of mechanisms indirectly through experimental probes—testing behavioral predictions, making lesions or pharmacologic interventions, and recording neural activity. It would be comforting if agreed-upon facts were not open to differing interpretation, but this state of affairs seldom exists. However, it is more important to *identify* agreed-upon experimental evidence than to seek consensus on what the evidence means. What, then, of experimental facts that are in dispute, and which disputes are most crucial to resolve? A good model and implementation scheme should tell us.

2. Neurobiological Background

Much of the difficulty in addressing questions of loci and mechanisms of learning arises from a reliance on lesion data and other indirect evidence. Although lesion data are vitally important, they have left workers in this field with some puzzles that will not be easily resolved. These unresolved issues are important for implementing neural network models of NMR conditioning in the brain. Before considering them, let us review the facts which I believe are *not* in dispute.

- Telencephalic brain regions and structures are not essential for acquisition, maintenance, or performance of the CR. Telencephalic regions that have been the focus of lesion studies include neocortex, hippocampal formation and other components of Papez circuit, basal ganglia, thalamus, and hypothalamus. At the midbrain level, lesion studies have shown that tectum, tegmental reticular formation, substantia nigra, and periacquiductal grey, to mention a few involved structures, are not essential for conditioning. The only essential midbrain structure identified to date is red nucleus (RN).

- Metencephalic brain regions, the cerebellum and brain stem are essential for the acquisition, maintenance, and performance of CRs. Within the metencephalon, researchers agree that the following subset of structures are essential for expression of *robust* CRs with normal topography: (a) Cerebellar cortex, specifically the region designated by anatomists as hemispheral lobulus VI (HVI); (b) cerebellar nucleus interpositus, specifically the anterior region (NIA); (c) magnocellular RN, specifically the portion that represents the facial region around the eye; (d) inferior olivary nucleus; specifically the dorsal accessory olive (DAO) which represents the facial regions around the eye and sends climbing fibers to HVI and NIA.

- Lesions that disrupt or eliminate CRs in one eye need not affect acquisition or performance of CRs by the other eye. Nor do such lesions interfere with the normal savings of trials to criterion when the US is no longer applied to the affected eye but is switched to the other eye. Since savings can be demonstrated, it is clearly the case that lesions do not impair some general capacity to acquire and store information.

- To a surprizing degree, lesions that disrupt or eliminate CRs do not affect the UR, although there may be small modulations of UR amplitude which are understandable in light of known anatomy and physiology.

- The reflex pathways mediating the CR and UR involve motoneurons that innervate the extraocular muscles, especially the retractor bulbi muscles. Most retractor bulbi motoneurons lie in the accessory abducens nucleus (AAN) and are innervated by nearby second-order sensory neurons of spinal trigeminal subnucleus pars oralis (SpoV). Although the brain stem components of these circuits have been well characterized both anatomically and physiologically, the nature and extent of the cerebellum's contribution remains an active area of research. There is strong evidence, outlined below, that the cerebellum makes a substantial *causal* contribution to the generation of CRs.

Workers in the extended laboratory of the conditioned NMR have proposed various test to determine whether CR-disrupting lesions or pharmacologic interventions involving critical metencephalic structures affect learning or performance. CR-disruption might be due to any number of factors unrelated to learning—these might all be subsumed under the heading "performance factors": (a) motor deficit, (b) sensory deficit, ruption of timing, (d) attentional deficit. Motor deficits can be eliminated as a cause of CR disruption to the extent that the UR remains unaffected (over a range of US intensities). Sensory deficits can be elimated to the extent that CRs are disrupted with different CS modalities. Attentional deficits can be ruled out the extent that CRs occur in the contralateral eye. Disruptions of timing can be assessed by varying the CS–US interval (Desmond and Moore, 1982).

Researchers do not agree on whether any of the above brain regions is involved in the actual learning process or, indeed, whether learning also depends on the integrity of other structures (Desmond and Moore, 1986). One possibility is that "learning the connection between a CS and the US" occurs within Purkinje cells (PCs) of cerebellar cortex, specifically at parallel fiber synapses. Contending views are that the critical connections are formed within the deep cerebellar nuclei or brain stem. It is well to get these issues in front of us before introducing implementation schemes. Thus armed, the reader can better judge their strengths and weaknesses. Some unresolved issues regarding the lesion data are reviewed here.

- Do the neural commands (motor programs) that result in a CR originate in the cerebellum? That is, can it be said that the cerebellum is a proximal *cause* of CR topography? We have recently peformed a linear systems analysis of the relationship between the firing rate of single neurons in NIA and the position of the NM during conditioning trials (Berthier, Barto, and Moore, 1988). Regarding a causative link, we find that in some NIA cells the relationship rate of firing and position of the NM can be modeled by a nonrecursive (causal) digital filter (Hamming, 1983). Using a related approach, we estimate the transfer function between neural activity and NM position, and from this it is possible to write a differential equation relating the two variables. Some NIA cells with CR-predictive firing yield equations for second-order systems. These equations relate a cell's firing rate to the acceleration, position, and velocity of NM movement. It is worth noting that NM movement is linearly related to eyeball retraction. In fact, the sweep of the NM over the eye is caused by retraction of the globe. The mechanics of eyeball retraction are those of a Voight element consisting of elastic and viscous components, a classic textbook example of a second-order linear system. Hence, it is perhaps not surprizing that equations relating the firing of some NIA cells to the conditioned NMR are those of second-order linear systems.

- Do lesions of cerebellar cortex produce a complete and permanent loss of a previously acquired CR? This question is important in itself, but especially so because of the well known theories of Marr (1969) and Albus (1971), who independently suggested that motor learning, including classical conditioning, involves cerebellar cortex in a fundamental way. Yeo and his colleagues were the first to show that HVI lesions disrupt CRs, typically by either eliminating them altogether or greatly reducing their amplitude (Yeo, Hardiman, and Glickstein, 1984). These studies have been extended to show that lesions of HVI must be complete in order to eliminate small amplitude responses that would normally be counted as CRs and to prevent recovery after extended post-operative training (Yeo and Hardiman, 1988). Lavond, Steinmetz, Yokaitis, and Thompson (1987) report small amplitude CRs and recovery following extended training in cases where HVI removal appears to have been complete, and so the issue remains in question.

- Do lesions of the inferior olivary nuclei cause a progressive decline of the CR resembling extinction as some investigators claim (McCormick, Steinmetz, and Thompson, 1985), or is it the case that such lesions merely disrupt normal functioning cerebellar in this way bring about an immediate detrimental effect on performance (Yeo, Hardiman, and Glickstein, 1986)? This issue is as yet unresolved because experiments have yielded conflicting results. If lesions of the inferior olivary nuclei, particularly DAO, do result in experimental extinction, then this would support models built on the idea that climbing fibers from DAO to cerebellum carry the reinforcement signal from the US to sites of learning.

- Does stimulation of the DAO provide a reinforcing signal for learning in cerbellar cortex (Steinmetz, Lavond, and Thompson, 1989)? Or is any learning in the cerebellum confined to NIA which receives climbing fiber collaterals from DAO? Related to this question is the possibility that stimulation of DAO does not reinforce learning in the cerebellum at all. It may merely stimulate brain stem elements of the reflex pathway underlying the UR where learning might occur (Bloedel, 1987; Yeo, 1989).

There are other issues to be resolved among workers in the extended laboratory of the conditioned NMR. I have mentioned only those that bear on evaluating the implementation schemes suggested for each of the models outlined in subsequent sections. Each model has its own implementation scheme. They both assume that learning occurs through Hebbian mechanisms which involve synaptic modification through convergence of CS and US information onto single neurons (Byrne, 1987). They both assume that these synaptic modifications occur in cerebellar cortex (HVI) and that CRs are initiated by the action of PCs on NIA cells to which they project. The implementation for the SBD model assumes that learning occurs in cerebellar cortex, but one synapse before the PC or output stage (Moore and Blazis, 1989). The other model, designated VET, is more complex and assumes that learning occurs within the brain stem as well as in cerebellar cortex. The cortical component assumes that learning occurs through modification of parallel fiber/PC synapses. In addition, it assumes that learning also occurs at the synapses of parallel fibers and Golgi cells (Moore, Desmond, and Berthier, 1989).

3. The SBD Model

The SBD model has been described in detail elsewhere (Moore, Desmond, Berthier, Blazis, Sutton, and Barto, 1986; Moore and Blazis, 1989) and so a brief summary will suffice. The model is based on a single neuron-like processing unit which receives input from many potential CSs and a US. The processing unit adjusts the weights (synaptic efficacies) of the CS input so that future output of the unit matches its current output.

Equation 1 specifies that the output of this system, denoted $s(t)$, equals the weighted sum of its input from potential CSs and the US. The variable $s(t)$ is a linear function of its weighted input only within an allowed range imposed by the fact that the NM can only move so far (about 10 millimeters) as the eyeball retracts. A CS's contribution to the output of the element is the product the current strength of its representation, denoted $x(t)$ in the model, and a corresponding "synaptic" weight denoted $V(t)$. Formally, the output of the system at time t, denoted $s(t)$, equals the weighted sum of input from all CSs, where $x_i(t)$

refers to the magnitude of CS_i, $i = 1, ..., n$, at time t:

$$s(t) = \sum_{i=1}^{n} V_i(t)x_i(t) + \lambda'(t). \quad (1)$$

$\lambda'(t)$ is the US's contribution to $s(t)$.

In Equation 1, $x_i(t)$ represents the activation level of the ith member of a set of potential CSs at discrete times t after onset (t represents successive time steps of 10-milliseconds duration). The following specifications for x_i were dictated by two contraints: (a) generation of realistic response topography for a forward-delay paradigm with a favorable CS–US interval, and (b) generation of realistic interstimulus interval (ISI) functions. The optimal CS–US interval for NMR conditioning is generally taken to be 250 milliseconds (Gormezano, 1972). When the CS_i begins, $x_i = 0.0$. It remains at 0.0 until $t = 7$, i.e., 70 milliseconds after CS_i onset. At this point, x_i begins to increase in an S-shaped fashion. It levels off to a maximum value of 1.0 by $t = 30$ (300 milliseconds after CS_i onset) and remains at this value until CS_i offset, at which time x_i begins to fall exponentially back to 0.0. Thus, according to Equation 1 the output of the model, $s(t)$, to CS_i conforms to the temporal map or *template* provided by x_i. As the number of training trials increases, the variable $V_i(t)$ increases, and the CR becomes increasingly robust. This process is reversed over a series of extinction trials.

Learning in the SBD model follows a modified Hebbian rule which states that changes of the synaptic weight of CS_i, ΔV_i, are proportional to the *difference* between the current output, $s(t)$, and the trace of preceding outputs, $\bar{s}(t)$. At time t, ΔV_i is computed as follows:

$$\Delta V_i(t) = c[s(t) - \bar{s}(t)]\bar{x}_i(t), \quad (2)$$

where c is a learning rate parameter, $0 < c \leq 1$.

The factor $\bar{x}_i(t)$ in Equation 2 specifies the degree to which the "synaptic junction" corresponding to CS_i is *eligible* for modification (Sutton and Barto, 1981). $\bar{x}_i$ is driven by the variable $x(t)_i$: After CS_i onset, it increases with the x_i, but with a lag of 30 milliseconds. It remains at full strength as long as the CS_i is on and begins to decay to a baseline value of zero 30 milliseconds after CS_i offset. The rate of this decay is inversely related to CS_i duration whenever CS_i exceeds 250 milliseconds.

Equation 2 does not contain an explicit term for the reinforcing action of the US. The US is important only insofar as it affects the term $s(t) - \bar{s}(t)$. The interaction the two time-dependent variables associated with CS_i, $x_i(t)$ and $\bar{x}_i$, together with $s(t) - \bar{s}(t)$, govern the rate of learning and shape of ISI functions. Trial-wise learning curves reflect accummulated net changes in V_i occurring *within* each trial. Such changes occur before and after the occurrence of the US. For example, given the 10-millisecond time step used in our simulations

(e.g., Moore et al, 1986), a trial with an ISI of 350 milliseconds might involve over 400 computations of ΔV_i.

The term $\bar{s}(t)$ in Equation 2 can be thought of as a short-term decaying trace of the system's output from previous time steps. Alternatively, it can be interpreted as a prediction or expectation of output based on previous output. It is computed as follows:

$$\bar{s}(t+1) = \beta\bar{s}(t) + (1-\beta)s(t), \tag{3}$$

where $0 \leq \beta < 1$.

Simulation studies indicate that, with a 10-milliseconds time step, optimal performance of the model requires that β be on the order of 0.6 (Blazis and Moore, 1987). Equation 3 with $\beta = 0.6$ also describes the inhibitory action of cerebellar Golgi cells on information flow through the granular layer of cerebellar cortex. This coincidence was exploited in implementing the model (Moore and Blazis, 1989).

The foregoing assumptions enable the SBD model to simultaneously generate response topographies and ISI functions for both trace and forward-delay conditioning paradigms (Moore et al, 1986). In addition, it retains the original Sutton-Barto model's ability to describe multiple-CS phenomena such as blocking, higher-order conditioning, and conditioned inhibition (Barto and Sutton, 1982; Sutton and Barto, 1981). In agreement with experimental liturature (Miller and Spear, 1985), the model does not predict extinction of conditioned inhibition.

3.1 Implementing the SBD model

Moore and Blazis's (1989) implementation of the SBD model is summarized in this section. We required that the implementation scheme meet the following criteria: (a) It had to involve the cerebellum and be consistent with its anatomy and physiology. (b) It had to account for the lesion data, namely the fact that lesions of cerebellar cortex (HVI) or associated brain stem circuits virtually elimiate the CR. (c) It had to propose neuronal loci where the learning rule (Equation 2) might be implemented. This meant proposing sites where CS information, the variable $\bar{x}$, convergences with the reinforcement signal, $s - \bar{s}$. (d) It had to propose schemes for computing $\bar{s}$ via Equation 3 and $s - \bar{s}$. The last item held the key. Once overcome, the rest of the implementation fell into place.

Turning now to the details of the implementation, the output variable s, which expresses the form of the CR and is used in the learning rule, is generated by the action HVI PCs on neurons in NIA to which they project. Evidence supporting this construction was reviewed above. Next, s is transmitted with high fidelity through each of the synaptic links leading to

AAN motoneurons and generation of the peripherially observed CR. One synapse before this stage, within SpoV, an efference copy of s peels off and ascends back to HVI via mossy fibers. This efference copy of s consists of two streams. One stream passes through the granular layer without modulation by Golgi cells. This stream gives rise to parallel fibers (axons of granule cells) that carry s information to other circuit components, including Golgi cells that modulate the other s stream. This modulation computes $\bar{s}$ and gives rise to parallel fibers carrying $\bar{s}$ information.

The existence of separate parallel fibers which carry s and $\bar{s}$ information allow for computation of the reinforcement factor in Equation 2. Golgi cells, different from those that compute $\bar{s}$, receive two simultaneous inputs: an excitatory input from $\bar{s}$-carrying parallel fibers and an inhibitory input from axon collaterals of PCs activated by s-carrying parallel fibers. Because Golgi cells are inhibitory neurons, the resulting action on granule cells to which they project is proportional to $s - \bar{s}$. In the implementation scheme, this output is directed to granule cells activated by CSs via mossy fibers. CS information has been preprocessed such that it expresses the variable, x. The eligibility factor, $\bar{x}$, presumably resides within x-activated granule cells. They are sites of convergence for implementing of the learning rule because they encode $\bar{x}$ and receive synaptic input encoding the reinforcement factor, $s - \bar{s}$, from Golgi cells.

Having computed ΔV, the output of these granule cells on the next computational step is proportional to Vx, which is also equal to the next value of s if we assume only one CS. Parallel fibers carrying Vx impinge on basket cells and PCs. The basket cells, which are inhibitory neurons, send axons to PCs on an adjacent group of parallel fibers. Increasing activation of basket cells causes the firing of these PCs to decrease below their baserate of firing in proportion to Vx. This decrease in firing disinhibits neurons in NIA to which they project, causing them to increase their firing rate and send an excitory pulse of activation through the efferent pathway which terminates in AAN.

3.2 Implication of the SBD model

The complexity of the implementation scheme stems from considerations of anatomy and physiology. These considerations are elaborated elsewhere (Blazis and Moore, 1987; Moore and Blazis, 1989). The most compelling evidence for the scheme comes from Berthier and Moore's (1986) study of how PCs in HVI respond during NMR conditioning.

Berthier and Moore (1986) recorded from single PCs in HVI during the asymptotic stages of two-tone differential conditioning. PCs with CR-related firing patterns could be classified as either increasing or decreasing their baserate of firing whenever a CR occurred. Three cells increased firing for every one that decreased firing. Firing patterns of PCs could also

be classified as either preceding or occurring simultaneously with CRs. All of the PCs that decreased their firing did so before the CR occurred, as would be necessary if their activity were responsible for initiating CRs. PCs which increased their firing before the occurrence of CRs are implied by parallel fibers carrying Vx information. PCs that increase their firing simultaneously with CRs are implied by the two streams of s-carrying efference from SpoV used in the computation of $\bar{s} - s$. It remains to be determined whether we can objectively discriminate increases in PC firing that mirrors s from that mirroring $\bar{s}$. This caveat aside, the frequency distribution of firing patterns observed by Berthier and Moore (1986) are accounted for by the implementation scheme.

3.2.1 Behavioral predictions

One prediction of the SBD model is that the rate of CR acquisition in a trace conditioning paradigm (but not a forward-delay paradigm) is an increasing function CS duration, provided the interval between CS offset and US onset (trace interval) is sufficiently long, e.g., 300 milliseconds or more. The prediction follows directly from the model's assumption that the eligibility factor in the learning rule, $\bar{x}$, decays at a rate which is inversely related to the duration of the CS. The prediction is counterintuitive because it states that acquisition can be faster with a longer-than-optimal ISI than one nearer to optimal. Preliminary studies with an acoustic CS (Blazis and Moore, 1989) have born out this prediction, but only when the CS is sufficiently intense (e.g., 80 dB). The prediction is not supported with a CS on the order of 60 dB. In this case acquisition rate appears to be dominated not by CS duration but as in forward-delay conditioning by ISI.

I mention this particular experiment in order point out that the SBD model does not yet provide a complete account of NMR conditioning. In this case, the model is incomplete because it says nothing about how CS intensity affects the variables x or $\bar{x}$. Part of the motivation for the above experiment was to obtain information on how to incorporate these effects into the model. The SBD model also fails to take account of processes that might occur within intertrial intervals, e.g., the "consolidation" effects from studies showing that rate of conditioning is a direct function of intertrial interval (Moore and Gormezano, 1977).

3.2.2 Physiological predictions

The most important prediction from the implementation scheme is that learning occurs within the granular layer of cerebellar cortex. Testing this prediction will require experiments on cerebellar slices using designs similar to those employed by Coulter and Disterhoft to investigate long-term effects of NMR conditioning on hippocampal pyramidal cells (e.g.,

Coulter, Lo Turco, Kubota, Disterhoft, Moore, and Alkon, 1989). It also remains to be proven that SpoV cells that fire in relation to CRs actually send *collateral* efference copy mirroring CR waveform to HVI. All we can say with confidence at this point is that cells in SpoV exist that show CR-related firing of the kind needed to provide HVI with a current copy of the variable s (Ricciardi, Richards, and Moore, 1989). We also know that some SpoV cells send mossy fibers to HVI. We no not know that the two categories actually overlap.

The implementation scheme does not assign a role in learning to climbing fiber inputs from DAO. Additional studies are needed to determine whether this is justified. One reason for discounting the possible contribution of climbings fibers is that their low firing rate makes them poor candidates for providing efference copy about s for implementation of the learning rule. In addition, very few PCs in the Berthier and Moore (1986) responded with a complex spike, indicative of climbing fiber input, when the US occurred. Nevertheless, the possibility that climbing fibers are important for learning cannot be ruled out without further experimental work (Moore and Berthier, 1987; Ito, 1989). In fact, Moore et al's (1989) implementation of the VET model, reviewed in the next secton, assumes that learning in the cerebellum is reinforced by climbing fiber input elicited by the US.

4. The VET Model

The SBD model is able to simulate response topography because it assumes that every potential CS provides the system with a fixed pattern of activation which serves as a template for the CR. We have speculated about how template may be formed and the the possible contributions of other brain regions, especially the hippocampus, in this process (Blazis and Moore, 1987). The fact remains that the SBD model basically sidesteps this issue. In addition, the SBD model is incapable of adaptively changing CR topography so as to simulate a number of paradigms. The SBD model cannot yield appropriate CR waveforms for the following cases:

- Trace conditioning. CR waveforms should peak just before the occurrence of the US, as in forward-delay paradigms, but the dynamics of the variable x do not permit this to happen. Instead, CR waveforms begin to fall toward baseline when CS offset occurs.
- Forward-delay conditioning with long CS–US intervals. The SBD model cannot simulate inhibition of delay. Since CR-waveform mirrors the template provided by the variable x, its latency and form are not influenced by CS–US interval.
- Multiple CS–US intervals. Training with multiple CS–US intervals yields complex CR-waveforms. For example, a study by Millenson, Kehoe, and Gormezano (1977)

showed that training with randomly mixed trials having CS–US intervals of 200 and 700 milliseconds gave rise to CRs with two peaks, each centered at a point of US onset.

The VET model overcomes these deficiencies. It is able to simulate appropriate CR waveforms for these cases because of features absent in the SBD model. These features include the following:

- CSs are provided with a temporal dimension through tapped delay lines which encode, not only the source of the stimulus, but also the time since the stimulus began. Another set of tapped delay lines encodes the time since the stimulus ceased. Hence, the model has timed-tagged input elements for both stimulus onset and offset (Equation 4).
- There are two neuron-like processing units that receive convergent input from CSs and the US. One unit (designated V) is the output device (Equation 5). It has modifiable synaptic weights which are changed according to an LMS rule resembling the Resorla-Wagner model (Equation 6). The main difference from the Rescorla-Wagner model is that weight changes depend on local eligibility factors (Equation 7), a global ISI parameter (Equation 8), and on an additional reinforcement signal reflecting the expected time of occurrence of the US (Equation 9).
- This additional reinforcement signal is computed by the other processing unit, designated the E unit, which learns when the US occurs. Like the V unit, the E unit receives convergent input from CSs and the US, and it has modifiable synaptic weights which are changed according to a simple linear difference equation (Equation 11) which includes local eligibility factors (Equation 10) and the global ISI parameter defined in Equation 8.

A more formal treatment follows:

Architectural assumptions for the network have been described in detail elsewhere (Desmond and Moore, 1988; Moore, Desmond, and Berthier, 1989). Basically, the onset and offset of each CS begin activation of separate tapped delay lines. The elements in the delay line are referred to as x_{ijk} elements because each element can be referenced by (a) its CS (i), (b) whether it is activated by the onset ($j = 1$) or offset ($j = 0$) of the CS, and (c) its number within the delay line (k). For example, element x_{208} belongs to the offset delay line for CS2, and is the eighth element activated in the delay line. The output of an x_{ijk} element (which is either 1 or 0) at time t is designated $x_{ijk}(t)$.

The x_{ijk} tapped delay line elements are activated sequentially, with a new element recruited every time step (10 ms). When activated, an x_{ijk} element changes value from 0 to

1, and remains at 1 for 10 time steps. Thus, for each trial beginning at time $t = 1$:

$$x_{ijk}(t) = \begin{cases} 1 & \text{if } \tau_{ij} + k - 1 \leq t < \tau_{ij} + k + 9; \\ 0 & \text{otherwise,} \end{cases} \tag{4}$$

where τ_{ij} is the onset time ($j = 1$) or offset time ($j = 0$) of CS i ($x_{ijk} = 0$ if CS i is not presented).

In addition to the x_{ijk} elements, the network has two higher-order processors designated the V unit and E unit. Each x_{ijk} element gives off two taps, one of which projects to the V unit and the other to the E unit. The latter connections are modifiable, and the weights for these connections are referred to as V_{ijk} and E_{ijk}. All other connections are non-modifiable; these include: US connections with the V and E units, an E-unit projection to the V unit, and connections between adjacent x_{ijk} elements in the delay line.

The output of the network, $s(t)$, is derived from the US input and from the weighted sum of the V unit inputs, and is defined as:

$$s(t) = \sum_i \sum_j \sum_k V_{ijk}(t) x_{ijk}(t) + L(t), \tag{5}$$

where $s(t)$ is confined to the closed unit interval.

Changes in the V_{ijk} weights are given by the following expression:

$$\Delta V_{ijk}(t) = c\{L(t) - \hat{s}(t)\} h_{ijk}(t) \overline{x}_{ij}(t) r(t). \tag{6}$$

where:

c is a rate parameter, $0 < c \leq 1$.

$L(t)$ is the reinforcement, $0 \leq L(t) \leq \lambda$, where λ is analogous to the strength of the reinforcement during conditioning, $0 < \lambda \leq 1$. $L(t) = 0$ until the US occurs, at which time $L(t) = \lambda$.

$\hat{s}(t) = \sum \sum \sum V_{ijk}(t) x_{ijk}(t)$, and is confined to the closed unit interval.

$h_{ijk}(t)$ constitutes an eligibility trace for each V_{ijk} synapse, $0 \leq h_{ijk}(t) \leq 1$. This term has maximum value at the onset time of the element and decays geometrically. It is computed as follows:

$$h_{ijk}(t) = \begin{cases} 1.0 & \text{if } t = \tau_{ij} + k - 1; \\ (0.8) h_{ijk}(t-1) & \text{if } t > \tau_{ij} + k - 1; \\ 0.0 & \text{otherwise,} \end{cases} \tag{7}$$

$\bar{x}_{ij}(t)$ is an *overall CS eligibility* for onset and offset processes, $0 \leq \bar{x}_{ij}(t) \leq 1$. This function governs the rate of conditioning that occurs at a given interstimulus interval. $\bar{x}_{ij}(t)$ is globally available to all V_{ijk} and E_{ijk} synapses. The equations described below approximate the empirically observed inverted-U-shaped function found in rabbit nictitating membrane conditioning:

$$\bar{x}_{ij}(t) = \begin{cases} (.05)(t - \tau_{ij}) - 0.25 & \text{if } \tau_{ij} + 6 < t < \tau_{ij} + 25; \\ (-1/475)(t - \tau_{ij}) + (500/475) & \text{if } \tau_{ij} + 25 \leq t < \tau_{ij} + 500; \\ 0.0 & \text{otherwise.} \end{cases} \tag{8}$$

$r(t)$ is the output of the E unit, and represents the temporal expectation of reinforcement, $0 \leq r(t) \leq \lambda$. It is defined as follows:

$$r(t) = \max\{E_{ijk}(t)\Delta x_{ijk}(t) \mid i = 1, \ldots, n;\ j = 0, 1;\ k = 1, \ldots, N\} \tag{9}$$

where:

$$\Delta x_{ijk}(t) = \begin{cases} 1 & \text{if } x_{ijk}(t) - x_{ijk}(t-1) = 1; \\ 0 & \text{otherwise,} \end{cases} \tag{10}$$

and E_{ijk} are the connection weights of the input elements onto the E unit. Changes in these weights are given by:

$$\Delta E_{ijk}(t) = c[L(t) - r(t)]\Delta x_{ijk}(t)\bar{x}_{ij}(t) \tag{11}$$

4.1 Implementing the VET model

The implementation criteria for the VET model were the same as for the SBD model. The two schemes share many common features, e.g., they both assume that CRs are generated by the disinhibiting action of HVI PCs on NIA neurons, and Golgi cells play a crucial role in both. The scheme assumes that the time-tagged input elements associated with a CS ascend to cerbellar cortex via mossy fibers. They synapse within the granule layer, and with no modulation are assigned to a corresponding set of parallel fibers. Note that the tapped delay line architecture exists outside the cerebellum, and their anatomical justification is discussed elsewhere (Moore et al, 1989). The parallel fibers which carry CS information synapse on both PCs and Golgi cells.

These synapses are modifiable. Synapses on PCs are sites where Equation 6 is implemented, and hence these cells are the V units. Synapses on Golgi cells are sites where Equation 11 is implemented, and hence these cells are the E units. Both sets of modifiable synapses are changed when the US occurs to the extent that they are eligible. The US triggers a climbing fiber volley which causes these synapses to undergo synaptic depression via

mechanisms of long term dression (LTD) identified by Ito (1989) and others. With learning, CS input causes V and E units to decrease their baserate of firing. For V units, this decrease initates a CR. For E units, this decrease disinhibits certain granule cells. These granule cells receive input from brain stem neurons, possibly in SpoV, which also undergo learning due to the convergence of CS and US information. Although no learning rule is specified, the SBD (or SB) model suffices provided the variable x in Equation 1 increases rapidly to a plateau at CS onset and decays slowly at CS offset.

With learning, the output (rate of firing) of these brain stem units consists of a short latency plateau which extends well beyond the offset of the CS. This output provides a uniform and long lasting stream of excitatory input to granule cells. The E units, however, gate this excitation and prevent it from exciting parallel fibers that synapse on the V units. As learning builds up in the E units, this gate is opened, but only during times near the expected occurrence of the US. Thus, E units provide the second reinforcing event necessary for modification of CS-input synapses on the V units so that they express appropriately timed CR waveforms.

4.2 Implications of the VET model

The VET model simulates virtually all of th behavioral phenomena encompassed with the SBD model, but unlike that model, it has the added feature of predicting realistic S-shaped acquisition curves. Unlike the SBD model, however, it cannot simulate second-order conditioning. As in the Rescorla-Wagner model, connection weights are strengthened only in the presence of the US. Desmond and Moore (1988) describe several novel predictions of the VET model. One prediction is that lengthening the duration of a CS after trace conditioning should result in double-peaked CR waveforms, reflecting contributions of both onset and offset tapped delay elements. The weights of offset elements are normally masked by those of the onset elements, but lengthening the CS exposes these offset elements, and CRs with two peaks emerge.

The physiological implications of the implementation scheme are many. The most interesting implication is the possibility that cerebellar Golgi cells express LTD at parallel fiber synapses in a manner analogous to that of PCs. There appears to be no evidence on this point in the literature. Another implication of the scheme is that climbing fibers from DAO do, in fact, reinforce learning. In order for this possibility to be taken seriously, it would be necessary to record from PCs (and Golgi cells) in HVI during the initial stages of CR acquisition. This was not done in the Berthier and Moore (1986) study, nor in any other study, for methodological reasons: It is virtually impossible to record from single neurons in an awake animal for the hundreds of trials normally required to obtain robust CRs. Never-

theless, there are ways around this problem we are pursuing in our laboratory. Finally, the scheme implies the existence of neurons in the brain stem that project to HVI and fire in accordance with the scheme's requirements. We have seen a number of candidate neurons in recordings from cells in NIA, RN, SpoV. Cells in RN and SpoV project to HVI, and it is possible, though not proven in rabbit, that NIA cells send mossy fibers to HVI as axon collaterals.

5. Concluding Remarks

The two models and implementation schemes are quite different, but not mutually exclusive. The VET model implies a neural network architecture which is well suited for forming appropriate CR waveforms for a wide range of circumstances. The output of this network need not be regarded as input to motoneurons. Instead, it could be regarded as a template used by another learning system responsible for such things as generating CRs and implementing second-order conditioning. Such a system might resemble the SBD model or some other supervised learning (error correction) algorithm.

Such a hybrid model would not encompasses phenomena which both models fail to address: intertrial interval effects, CS intensity, stimulus generalization and discrimination. These phenomena require a richer respresentation of CS input to learning networks than have been considered by either model too date. Desmond (1988) has developed one approach which can potentially address these topics. It represents CSs as planar arrays of elements through which activation spreads and decays in an orderly, yet stochastic manner. The planar array approach follows directly from the foundations provided by the SBD and VET models, and we might anticipate as abundant a harvest of interesting implications as have sprung from its forerunners.

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Single-unit activity in the rabbit red nucleus during the classically conditioned nicititating membrane response: A preliminary report

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Introduction

Previous investigations of the rabbit nictitating membrane (NM) response have implicated the red nucleus (RN) in the control of the conditioned response (CR). Lesions of RN or the rubrobulbar tract produce deficits in contralateral, but not ipsilateral CRs (Haley, Lavond and Thompson, 1983; Rosenfield and Moore, 1983; Rosenfield and Moore, 1985; Rosenfield, Dovydaitis, and Moore, 1985). HRP administration in the region of the accessory abducens nucleus (AAN), the nucleus primarily responsible for defensive eyeball retraction, results in labeling of contralateral RN neurons (Desmond, Rosenfield, and Moore, 1983). In cats, stimulation of RN produces EPSPs in contralateral AAN neurons at monosynaptic latencies (Grant and Horcholle-Bossavit, 1986). In light of evidence that cerebellar deep nuclei (Clark, McCormick, Lavond, and Thompson, 1984; Yeo, Hardiman, and Glickstein, 1985a), cerebellar cortex (Berthier and Moore, 1986; Yeo, Hardiman, and Glickstein, 1985b, but see Lavond, Steinmetz, Yokaitis, Lee, and Thompson, 1986) and inferior olive (McCormick, Steinmetz, and Thompson, 1985; Yeo, Hardiman, and Glickstein, 1986) are involved in CR control, and given that RN receives major input from cerebellar deep nuclei, it appears likely that RN is one component of a cerebellar–brain stem circuit. The purpose of this experiment was to record the activity of single RN neurons from awake rabbits during classical conditioning training (of the contralateral eye) and observe whether CR-related unit activity was elicited.

Methods

The training procedures were similar to those described by Desmond and Moore for recording in the dorsolateral pontine tegmentum (Desmond and Moore, 1986). We used a differential conditioning procedure in order to obtain trials with and without CRs. CS+ and CS- were 1200 or 600 Hz tones (counterbalanced) of 350 ms duration and 75 dB intensity presented in a pseudorandom sequence. White noise of 65 dB intensity was on continually. The US, an electrostimulation of .05–0.5 ms duration and 1 mA intensity delivered to the periocular region of the right eye, coterminated with the CS+. The intertrial interval was 20 s. The rabbits were trained for 2–3 days (100 trials/day) and then surgically prepared for unit recordings. The rabbits were anesthetized with a ketamine (40 mg/kg) – acepromazine (1 mg/kg) mixture (i.m.). A small recording hole was drilled on the left side of the skull, and 3 additional holes were drilled for anchor screws. A recording chamber was cemented in place and the rabbit was allowed to recover for 2 days.

For unit recordings, the head of the rabbit was held motionless by fastening the recording chamber to a support bar. A tungsten microelectrode of 1-5 MΩ impedance was lowered into

the brain stem during presentation of CS+ and CS- trials. Unit activity and NM movement were taped for offline analysis. Recording sites were marked at the end of the session by passing cathodal current (20 μA for 10 s) through the recording electrode. A maximum of 3 recording tracks were made for each rabbit. The rabbits were then sacrificed with sodium pentobarbital and transcardially perfused for subsequent histological identification of the recording tracks.

For data analysis, tape recorded neuronal activity and NM responses were digitized using an Apple IIe microcomputer. Spikes were window discriminated; the time of occurrence of each spike, relative to the trial onset, was recorded to the nearest 250 μs. The NM response was sampled at 200 Hz. The data were then transferred to a Sun 3/50 workstation for subsequent analysis.

Results

A total of 195 cells were recorded from 24 New Zealand albino rabbits. The 137 cells judged to be located in the appropriate region were grouped as follows: 45 cells exhibited unit activity that was strongly correlated with the CR, 26 displayed moderately correlated activity, and 66 showed little or no CR-correlated activity. The 45 cells showing strong CR-correlated activity could be grouped into three major types.

Type I (N = 22). These cells exhibited an increase in firing rate during the execution of the CR. The onset time of the increase was correlated with the onset time of the CR (mean $r = 0.67$, S.D. = 0.18.) The measure Δ^2, as recommended by Commenges and Seal (Commenges and Seal, 1986) was ≤ 1 for each cell. These cells could be further subdivided into two groups:

1. Cells with very low baseline firing (mean = 2.52 spikes/s, S.D. = 2.45, N = 11).
2. Cells that were spontaneously active (mean = 30.82 spikes/s, S.D. = 12.38, N = 11).

Neuronal firing patterns for 2 Type I cells are depicted in Figure 1 (one cell/row). For each cell there are two graphs. The left-side graph, which will be referred to as a peri-stimulus plot, depicts from top to bottom, NM responses in order of onset latency, spike raster plots, and spike counts collected in 5 ms bins. Vertical lines indicate the onset time of the CS and the US (on nonreinforced trials the US line indicates CS offset). Spike activity prior to CS onset represents baseline firing. The label in the top left corner indicates the type of CS

(600 or 1200 Hz) and whether or not a US was present (+ or -). A label of CR indicates that CR trial types from both CS+ and CS- were pooled. The right-side graph, which will be referred to as a peri-event plot, depicts spike and NM responses for CR trials only; NM responses and spike activity are shifted so that CR onset times are aligned. Calibration marker represents 100 ms (X-axis) and 100 spikes/s (Y-axis) for all graphs.

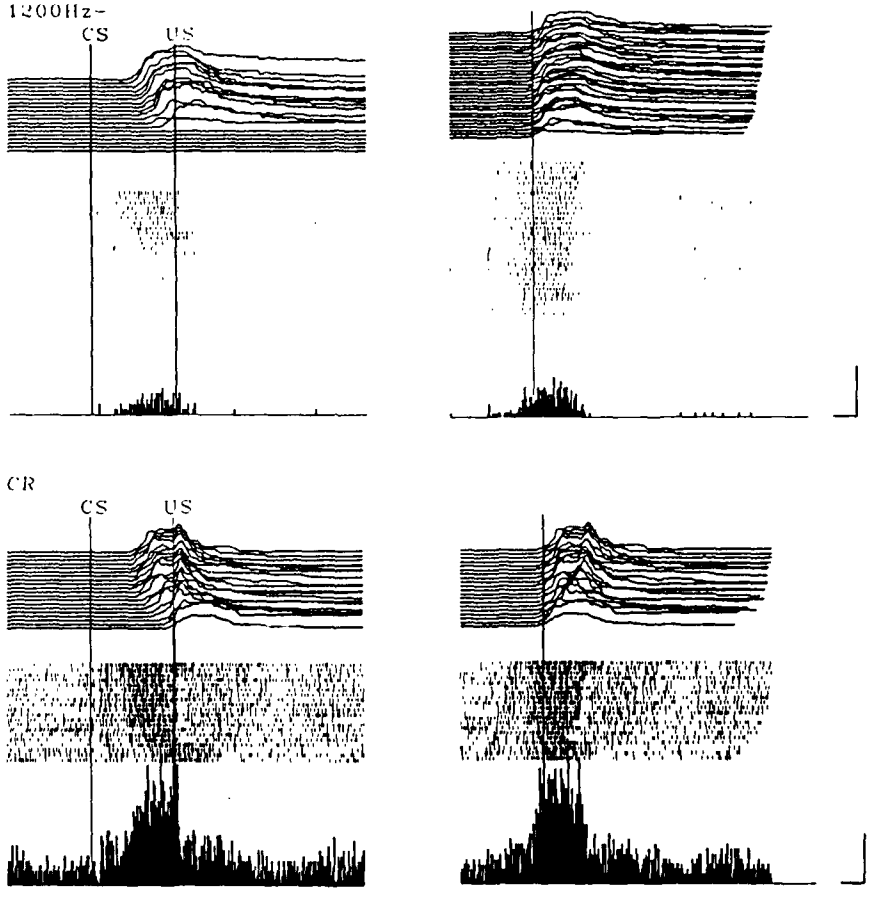

Figure 1: Two examples of Type I cells. For each cell, neuronal activity and behavioral responses are depicted in a peristimulus time histogram (left side) and a peri-event histogram (right side).

Type II (N = 15). These cells also exhibited an increase in firing rate during CR execution, but the onset of the neural burst was not correlated with the onset time of the CR (mean $r = 0.13$, S.D. $= 0.21$, $\Delta^2 > 1$). Examples of firing patterns for Type II cells are given in Figure 2. Typically, these cells increased firing shortly after CS onset and increased further during the CR. These cells could also be divided into two groups:

1. Cells with very low baseline firing (mean = 2.12 spikes/s, S.D. = 1.85, N = 9).
2. Cells that were spontaneously active (mean = 25.55 spikes/s, S.D. = 14.66, N = 6).

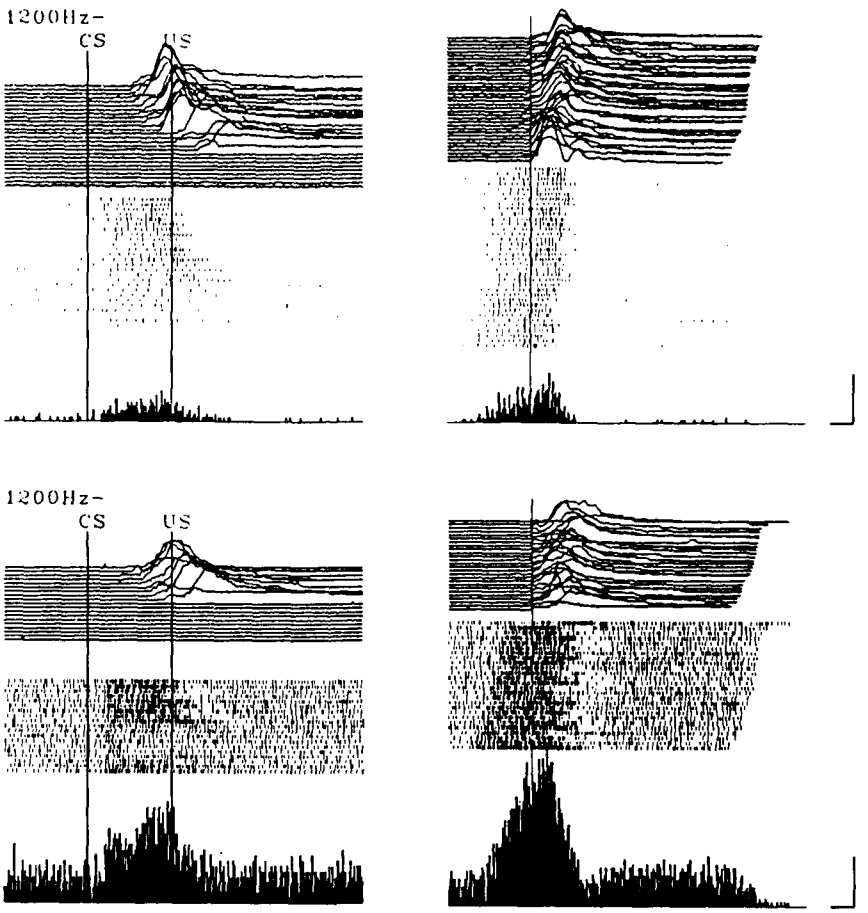

Figure 2: Two examples of Type II cells.

Type III (N = 8). These cells exhibited CR-related decreases in firing rate. The mean baseline firing rate for these cells was 23.83 spikes/s, S.D. = 10.12. Examples of two Type III cells are given in Figure 3.

A total of 14 cells displayed both increases and decreases in firing after the US occurred. Many of these cells were located in or in close proximity to the magnocellular division. Examples of US responses in 2 of these cells are illustrated in Figure 4.

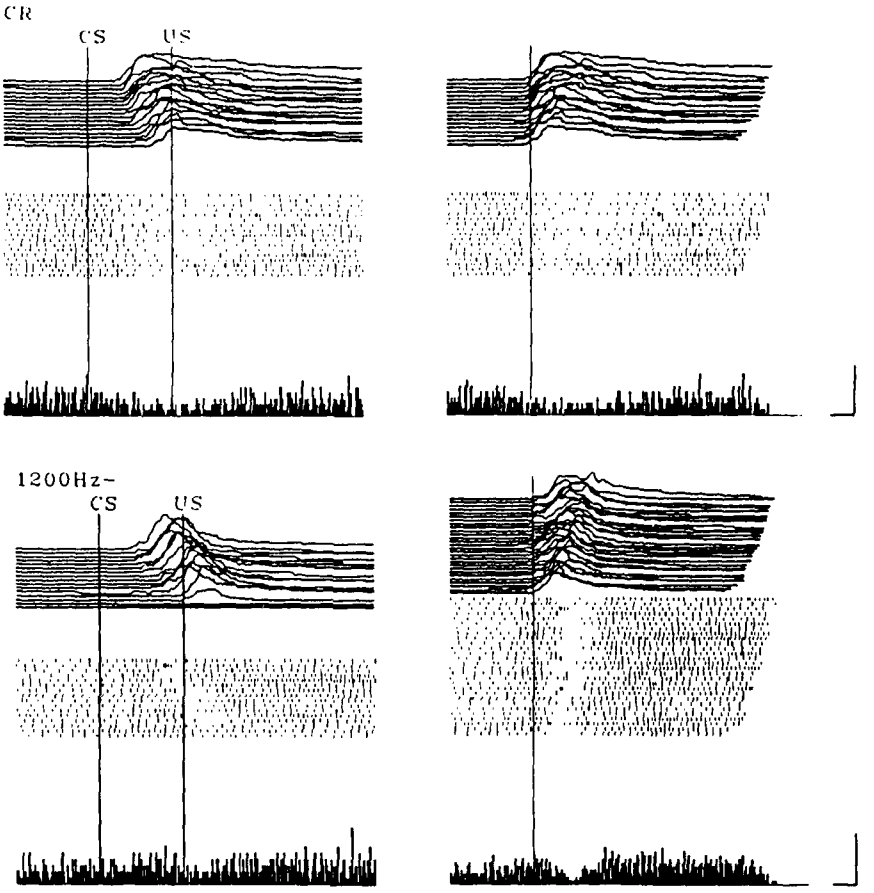

Figure 3: Two examples of Type III cells.

To determine the temporal relationship between neural activity and the behavior, we inspected peri-event plots, which were described above, and graphs showing the cumulative sum of spike counts adjusted for baseline firing (Ellaway, 1977; Gibson, Houk, and Kohlerman, 1985). The latter graphs were constructed using the algorithm, $y(t) = \sum_{i=1}^{t}[x(i) - \overline{x}]$, where $y(t)$ is the cumulative sum at time bin t (10 ms bins were used), $x(i)$ is the number of spikes in time bin i, and $\overline{x}$ is the mean number of spikes per bin computed from the pre-CS period. In these graphs, changes in firing rate are depicted as changes in slope of the line, where 0 slope denotes baseline firing. For Type II cells we tried to differentiate the initial neural burst at CS onset (which occurred for both CR and non-CR trials) from a later CR-specific discharge. The latter discharge was identified by a second change in slope in the graph; neuronal lead time was measured from this point.

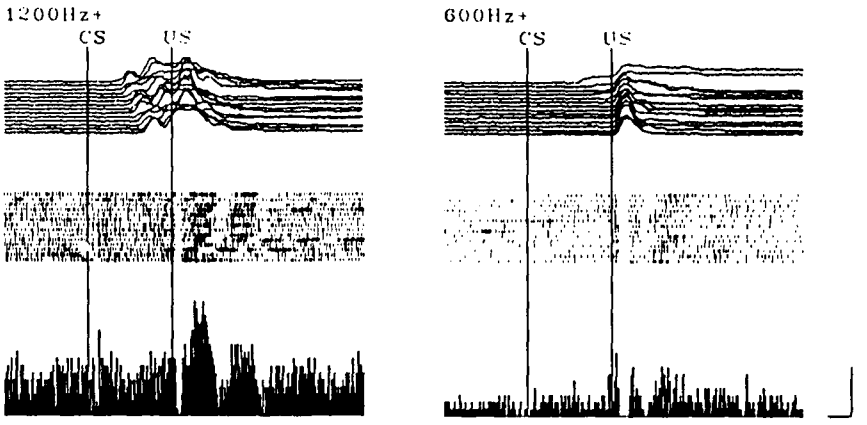

Figure 4: Examples of complex neuronal responses to the unconditioned stimulus.

The results of these temporal analyses are depicted in Table 1, which shows the average time in ms by which change in neuronal firing preceded the onset time of the CR for each cell type. "Quiet" and "Active" refer to baseline firing rates.

Recording locations for all cells in this experiment are depicted in coronal sections in Figure 5. Numbers in the bottom right corner of each panel indicate the distance in mm rostral to the most posterior pole of the magnocellular RN. The region where most magnocellular RN cells are found is indicated in each section (see mRN label in 0.50 section). This region is depicted with a dotted line at the 2.5 mm section because the large cells are more diffusely located at this level. The parvicellular division is difficult to precisely delimit, but

Cell Type	Mean	S.D.	N
Type I Quiet	60.5	37.9	11
Type I Active	70.9	33.6	11
Type II Quiet	52.8	34.5	9
Type II Active	58.3	34.9	6
Type III	30.6	60.2	8

Table 1: Time by which changes in neuronal discharge preceded the onset of the conditioned response for each cell type. Mean and standard deviation of the lead times (in ms) as well as sample size are reported.

it extends both laterally and dorsally from the magnocellular border (Gerhard, 1968).

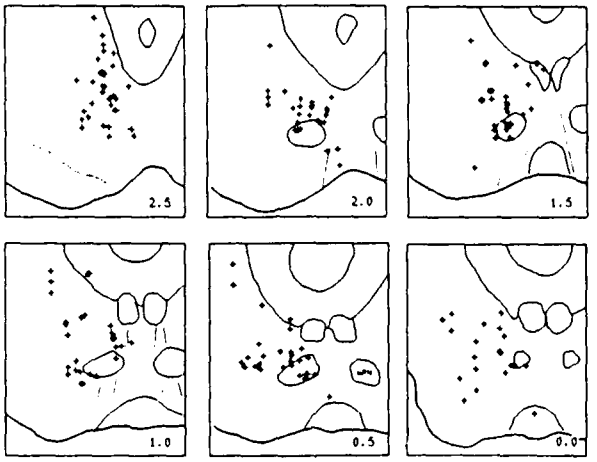

Figure 5: Anatomical locations of all recording sites in this study. Numbers at the bottom right of each section represents the distance in mm rostral to the posterior pole of the magnocellular RN.

Locations of strongly CR-correlated Type I, Type II, and Type III cells are illustrated in Figures 6, 7, and 8, respectively. These figures show that many, but not all, Type I cells tend to be found near the dorsal border of the caudal magnocellular RN. However, there is considerable overlap in the anatomical distributions of the three cell types.

Conclusions

We have found that CR-related changes in neuronal activity in RN is manifested primarily as increases in firing rate that precede the behavior by approximately 50-70 ms. Cells that fired in this manner were divided into two types. Type I cells appeared to be highly movement related, and consistently fired prior to the onset of the CR. Type II cells were not as well correlated with movement. Many of these cells increased firing shortly after CS onset, and thus, the activity of these cells appeared to have a sensory component. However, comparisons of neural activity on CR versus non-CR trials for these cells suggests that their activity also has a movement component. CR-related decreases in firing (Type III cells) were less often encountered, and usually followed the onset of the behavior.

Based upon the sample gathered thus far, Type I cells with active baseline firing may be more closely associated with the magnocellular division of RN than Type II or Type III

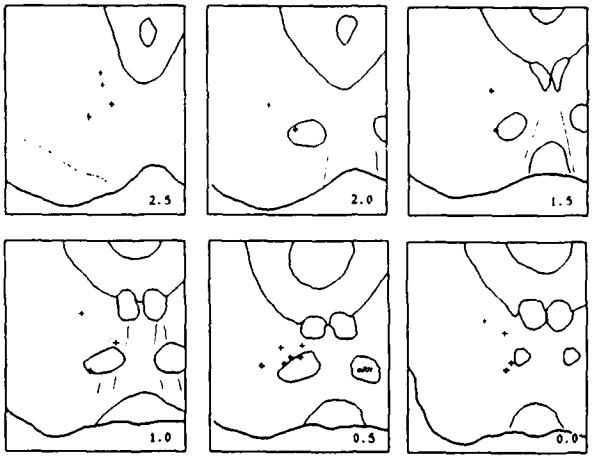

Figure 6: Locations of all stongly CR-correlated cells that were classified as Type I. Cells that exhibited quiet (+) and spontaneously active (*) baseline firing are depicted. Changes in neuronal activity preceded CR onset in all but one of these cells.

cells. Most of the recordings that were in the magnocellular division tended to be located at caudal levels of the nucleus and at the dorsal and lateral edges. Type I and Type II cells having low baseline firing rates tended to be located dorsal to cells that were spontaneously active. These quiet cells were presumed to be in the parvicellular division of RN as delimited in Gerhard's atlas (Gerhard, 1968).

The results of this experiment are consistent with RN involvement in CR control. Based upon physiological and anatomical evidence in cats, descending projections from RN could influence contralateral accessory abducens motoneurons either directly (Grant and Horcholle-Bossavit, 1986) or via trigeminal relay (Edwards, 1972; Robinson, Houk, and Gibson, 1987).

Acknowledgements

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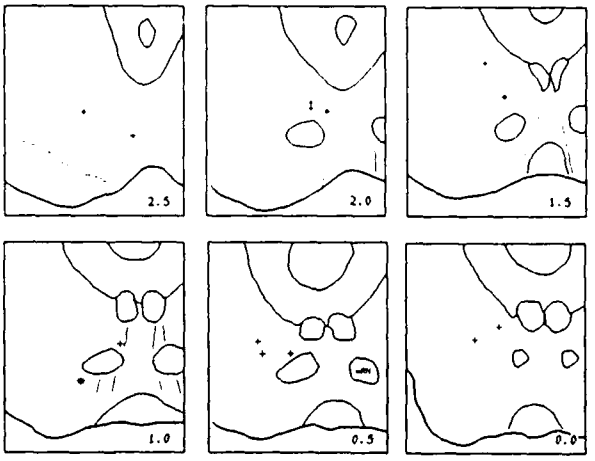

Figure 7: Locations of all stongly CR-correlated cells that were classified as Type II. Cells that exhibited quiet (+) and spontaneously active (*) baseline firing are depicted. Changes in neuronal activity preceded CR onset in all but one of these cells.

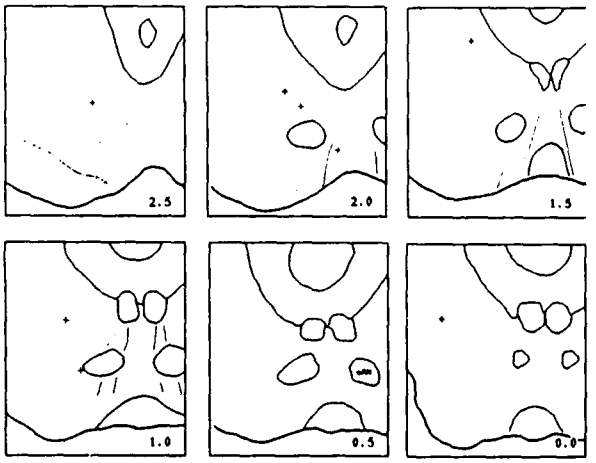

Figure 8: Locations of all stongly CR-correlated cells that were classified as Type III. Decreases in firing preceded CR onset in only 3 cases (*). The remaining 5 cells exhibited decreases in firing after CR onset (+).

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